





**SAJOUS'S**  
**ANALYTIC CYCLOPEDIA**  
**OF**  
**PRACTICAL MEDICINE**

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**SUPPLEMENT**



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## PREFACE

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SINCE the last Supplement to Sajous's Cyclopedia of Practical Medicine appeared, unusual progress has been made in the various fields of medicine and surgery. Research of all kinds, including that which is concerned especially with the clinical aspects of medicine, has never been so widespread nor so fruitful as during the past two years, in the course of which a large amount of work has been produced of scientific merit and practical value. As a consequence, the medical literature of all countries has never contained so much that is of essential importance to all who would keep well informed about the various branches of medicine.

In this SUPPLEMENT, as in the last, it has not been our aim to attempt to furnish a *complete* analysis of the entire medical literature for these years. The futility of such an undertaking is as apparent as its value is dubious. We have sought, rather, to produce a well-balanced volume devoted to a critical review of those subjects in medicine, surgery and the medical sciences in which noteworthy progress has been made or in which advances of practical value have occurred. This has been accomplished through the cooperation of the group of contributors, whose names appear elsewhere, who have so ably supplemented the efforts of the Editorial Board, especially in dealing with topics of a more highly technical character. In every instance, the subject selected for discussion has been assigned to a reviewer whose special training and broad experience in that particular field made it possible for him to exercise unusual critical judgment in the preparation of an authoritative contribution. The advantage of such a plan in the preparation of a Supplement of this kind, is self-evident when the present highly specialized state of medical science is considered.

The general arrangement and form of the present SUPPLEMENT differs but little from that of the earlier ones. In order to facilitate quick reference, the various subjects have again been arranged alphabetically. Less small type has been employed than formerly, while bold type has again been used to insure additional prominence for therapeutic procedures.

Although an earnest effort has been made not to neglect or overlook any subject of importance, it is too much to hope that no such omissions have occurred. On the other hand, many subjects that have received unusual

attention in recent years from research workers and clinicians alike, have been dealt with in considerable detail and at some length

In this category should be mentioned tuberculosis, which has been extensively reviewed from its newer immunological aspects as well as from a clinical standpoint. Syphilis has also been accorded prominence. The ever-changing opinions as to the most effective method of managing this infection have been discussed and the newer experimental and bacteriological advances emphasized. In the field of gastroenterology, such live topics as the various types of colitis, tests for liver function, diseases of the biliary tract, pancreatic disorders and gastroduodenal ulcer, in all its controversial aspects, have been stressed. An especially valuable review of literature on radium has been furnished because of our rapidly changing conceptions of this subject and its ever-increasing therapeutic importance. In the field of pediatrics, infant feeding, malnutrition, diseases of the newborn, and scarlet fever have been discussed at length. Under the heading "Cardiovascular System," a complete discussion will be found of the most recent advances in cardiac physiology and diagnosis, as well as angina pectoris and coronary thrombosis, rheumatic and syphilitic heart diseases and their management. The latest developments in abdominal and, under tuberculosis, thoracic surgery, together with present day views on anesthesia, the management of fractures, the surgery of the kidney, blood transfusions and the treatment of uterine and ovarian tumors, may be cited as a few of the outstanding surgical topics dealt with. Under the more restricted specialties of ophthalmology and otolaryngology, amblyopia, glaucoma, disorders of the conjunctiva and cornea, blindness, and diseases of the optic nerve under the former and endoscopy and diseases of the larynx under the latter, deserve comment. The complications and disorders of pregnancy, sterility and uterine diseases have been reviewed. The kaleidoscopic changes in endocrinology, and particularly the noteworthy work that has been done on the sex hormones and the adrenal cortical hormone, are adequately discussed. Disturbances of the thyroid, as well as the most recent researches on diabetes, obesity, and other metabolic disorders are also critically reviewed. Some of the less common conditions, such as Jamaica ginger paralysis are likewise included. An unusually extensive review of the recent literature on cancer has been prepared. Pneumonia, atelectasis, allergy, pernicious anemia, bacteriophage, and asthma have also been accorded considerable prominence.

The above subjects have been enumerated because they are of especial interest, but no attempt has been made here to summarize or even mention all of the subjects that the Editors and Reviewers have deemed of sufficient importance to merit detailed consideration in the present SUPPLEMENT

Finally, the Editor wishes to express his appreciation of the help and cooperation which he has received from the Editorial Board and from all of the Reviewers, whose interest and diligence have made possible the early publication of this volume, the value of which is largely dependent upon the excellence of their contributions. His thanks are especially due to the Assistant Editor, Dr Edward L. Boitz, who not only in large part planned the scope of this SUPPLEMENT, but also has contributed liberally to its pages. He is also indebted to Dr J. Warren Hundley for valuable assistance in reading the proof. The Editor is under many obligations to Miss L. I. Weisgerber for her aid in preparing the manuscripts, and the admirable way in which she has compiled the Index. The Publishers, who have so consistently cooperated with the Editor and his Associates, are to be congratulated on the excellent appearance of this volume.

GEORGE MORRIS PIERSOL



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# SAJOUS'S ANALYTIC CYCLOPEDIA of PRACTICAL MEDICINE

## SUPPLEMENT

### A

#### ABDOMEN, ACUTE SURGICAL, IN CHILDREN.—DIAGNOSIS

—According to W E Ladd (Pennsylvania M J 34 153 (Dec) 1930) one of the most common abdominal conditions in children is *congenital pyloric stenosis*. The symptoms usually start in the third week of life with the projectile ejection of vomitus containing ingested food and gastric secretions but no bile. The stools become scanty and are composed of bile, mucus, and intestinal secretions. The infant loses weight and becomes dehydrated. On physical examination, peristaltic waves may be seen in the epigastrium. They run from left to right, except just before vomiting, when they become reversed. On palpation, an olive-shaped tumor may be felt just to the right of the midline in the region between the liver and the umbilicus. Relaxation of the abdominal muscles for palpation is best obtained by giving sufficient water to cause vomiting. The moment just before the occurrence of vomiting the pyloric tumor can be felt readily. This method is preferred to the administration of a barium meal and x-ray examination for, if surgical interference becomes necessary, convalescence is hindered by the barium.

Among the rarer conditions which may complicate the diagnosis of pyloric

stenosis are atresia and stenosis of the duodenum. In intestinal obstruction the abdomen will not be distended if the obstruction is high and the vomiting effective.

*Intussusception* is an acute emergency of childhood. Early diagnosis is essential. The condition occurs in the sixth or seventh month of life. The onset is sudden and associated with crying, severe abdominal pain, pallor, sweating, and nausea or vomiting. The pain is paroxysmal. Between the spasms, when peristalsis is inactive, the infant appears perfectly well. The invagination usually starts at the ileocecal valve. At the onset, the tumor is usually in the right side. A few hours later it may pass up under the liver margin where it is difficult to palpate. Abdominal distention does not become marked until late in the condition, when fecal vomiting and fever occur and the mass can be palpated only by rectal examination.

*Meckel's diverticulum* may have features in common with intussusception or may be the cause of it. Of the author's series of 28 cases, blood was found in the stools in over 50 per cent.

The most common abdominal disease due to bacterial infection which occurs in childhood is *appendicitis*. This condition develops most frequently between the sixth and eleventh years. Before

the third year it is rare. The first symptom is pain which may occur in the right lower quadrant or may be referred to the epigastrium or the umbilical area. In some cases, because of the relatively greater length of the appendix and mesocecum in the child, it may be felt in the pelvis. It is soon followed by nausea or vomiting, leukocytosis and fever. The usual temperature is from 100.5° to 102.5° F (38° to 39.1° C). A temperature over 103° F (39.4° C) is sufficiently rare to suggest that the diagnosis is incorrect.

*Pyelitis* is often confused with appendicitis. An acute attack is frequently ushered in by nausea, vomiting, and a moderate degree of abdominal distention. The temperature is usually higher than in appendicitis. During the first 48 hours there may be little or no pus in the urine.

*Pneumonia*, usually central or situated in the lower lobe near the diaphragm, may present symptoms suggesting abdominal disease. While it is frequently diagnosed as appendicitis, it is characterized by rapid and labored respiration and a higher temperature than is found in abdominal conditions. Gradual firm pressure produced by the hand tends to relieve the spasm and decrease the discomfort, whereas in peritoneal inflammation it has the reverse effect.

Other less frequent abdominal conditions in children are *acute mesenteric adenitis*, *primary peritonitis*, *retroperitoneal iliac abscess* (not psoas abscess), and *malformations of the urinary tract*.

**ABDOMEN, INJURIES OF.—**  
**CONTUSIONS.**—J. Leveuf (Bull et mém Soc nat de chir 56 1143 (Nov 8) 1930) comments on a case of abdominal contusion with intestinal disinsertion of the mesentery, which was

observed by Carajannopoulos. The patient had been in an automobile accident and was badly shaken, although his abdomen had not been struck directly. There were no obvious signs of an intestinal lesion. After a few days, however, slight pain produced by palpation in the region of the right iliac fossa and a slight contraction at the painful point became gradually more marked. At the same time the Douglas *cul de sac* gradually became filled with fluid. On the strength of these symptoms, surgical intervention seemed expedient. The mesentery was found to be completely detached from the intestine in 2 places. The patient was cured by **resection of the 2 gangrenous parts of the intestine and end-to-end anastomosis**.

Esau (Zentralbl f Chir 56 2697 (Oct 26) 1929) relates the case of a man who fell downstairs, landing on a broom handle which caused a slight external injury of the skin in the perineal region. He arose and walked home without serious discomfort. Twelve hours later he developed symptoms indicative of rupture of the intestine. On examination only the slight skin wound was found. At operation 2 large tears of the intestine were discovered but without any opening in the peritoneum, nor was there any injury of any of the pelvic organs. There was no communication between the perineal skin wound and the interior of the abdominal cavity. Appropriate **suturing** was done and the patient made an uneventful recovery.

**Stomach.**—F. E. Bolton (Brit M. J. 2. 1005 (Nov. 30) 1929) reports a case of *traumatic rupture* of the stomach without any sign of injury to the abdominal wall. The patient fell from a ladder and was struck in the lower part of the abdomen by a piece of iron pro-

jecting about 12 feet below. He had had a full meal about  $1\frac{1}{2}$  hours previously. There were signs of shock, and the pulse was 92. The abdomen generally was held rigid but was not boardlike, and the patient sat up to take off a tight garment. There was no dullness in the flanks. Liver dullness was present, and there was no hyperesthesia to pain reflex. Pain was referred to the lower part of the abdomen and radiated down to the testicles. Clear urine had been passed 20 minutes before examination. Bolton decided to wait for further signs, after  $5\frac{1}{2}$  hours the pulse rose to 120, there were distinct signs of tympanites, and the leukocyte count was 15,300. He was therefore given a general anesthetic and the abdomen was opened. A hole with everted mucous membrane, and easily admitting the forefinger, was found on the anterior surface and near the greater curvature in the pyloric end of the stomach. There were no signs of any ulcer present, nor any signs of injury to any other viscus. The hole was sewed with Lembert over primary deep sutures, a peritoneal toilet was performed, and a drainage tube was placed in the under surface of the liver. The patient eventually made a good recovery.

**Spleen.**—H. Bailey (Brit J Surg 17 417 (Jan) 1930) reports a case of *spontaneous rupture* of the spleen and reviews 11 other cases from the literature.

Bailey's patient, a man 20 years of age, was suddenly seized with pain in the abdomen and left shoulder while he was sitting in a chair. His temperature then rose to  $101^{\circ}$  F. ( $38.3^{\circ}$  C) and his pulse rate to 100. Examination revealed generalized abdominal tenderness. This was maximal in the right hypochondrium where rigidity was also

found. Laparotomy disclosed a large amount of free blood. **Splenectomy** was performed. A subcapsular hematoma had ruptured.

In conclusion, Bailey states that in a traumatic hemoperitoneum in the male the spleen should be examined first.

P Goinard (Bull et mem Soc nat de chir 56 916 (July 12) 1930) discusses the cases of 4 men in whom severe abdominal injury was associated with wounds of the spleen and left kidney. The wound of the spleen in 3 cases had determined an intraperirenal hematoma. The condition of the organs was such that **splenectomy** and **nephrectomy** were necessary. Rapid death ensued in 1 instance. In the fourth case, the wound in the spleen with internal hemorrhage was treated by splenectomy. There was also hematuria, due to a subcortical renal lesion. There was no perirenal hematoma. The patient died after 3 weeks as the result of postoperative pulmonary complications. The author suggests the following 3 possible types of incision: a lumbar incision, a transverse abdominal incision, and a median laparotomy incision.

According to R. Desjacques (Lyon chir 27 17 (Jan-Feb.) 1930), the literature gives the impression that *traumatic lesions of the spleen and the left kidney are frequently associated*. This conclusion is based on the results of autopsies, as the 2 lesions usually occur in the extremely severe cases in which there is no opportunity to operate. In some cases the lesion of one of the organs does not require operation and recovery follows treatment of the other organ. Of most interest are the cases of associated lesions of the kidney and of the spleen in which both organs must be treated actively. Desjacques cites cases in which death followed operation.

on only one of the injured organs and others in which it followed an operation in which both organs were treated. Recovery after the removal of both organs is uncommon.

When the *diagnosis* is not certain, a median incision above and below the umbilicus supplemented, if necessary, by transverse opening toward the splenic region, is convenient. When the diagnosis of splenic rupture is certain, the transverse incision and the Mayo incision are satisfactory.

The author reports a case of a girl 7 years of age who fell from the second story. The fall was followed by signs of internal hemorrhage and hematuria. The spleen had been ruptured and the left kidney had burst. **Splenectomy** and **nephrectomy** were followed by recovery. The spleen showed no signs of an earlier lesion.

**Kidney.**—G. S. Epstein (J. d'urolog. 29.31 (Jan.) 1930) reports 8 cases of subcutaneous *rupture* of the kidney due to trauma, dividing these cases into 3 clinical groups: serious cases which necessitate immediate operation, less serious cases, and those of simple clinical evolution. Invariably the injury can be diagnosed through hematuria and the formation of a tumor. In *severe cases* the **kidney** should be **resected immediately**, although it is advisable to perform a function test of the other kidney before operating or during the operation. A *second group* causing *hematuria* and *tumefaction* is not of immediate danger to life and results in the formation of adhesions. Epstein favors **expectant treatment** and operates only if the symptoms become aggravated.

**ABDOMINAL PAIN.**—W. C. Alvarez (Am. J. Surg. 14:385 (Nov.) 1931) is concerned about the patient

who has persistent abdominal pain in spite of having had operations upon his appendix, gall-bladder, stomach, and other intraabdominal organs with no improvement of symptoms. Just as the facial surgeon, when dental extraction does not cure facial tic douloureux, turns to sensory nerve destruction so does Alvarez attack the problem of treating abdominal pain in its various pathways and blocking it when other procedures have been of no avail.

The patient frequently forces the more radical efforts on the part of the surgeon to free him from pain. He eventually loses all confidence in medicines and diets, but will take any risk in the hope of painless life or death.

The work done along the lines of neurosurgery in the effort to relieve the pain of angina pectoris, which has had some success throughout the world, increases the desire to promote research directed toward relieving, blocking, or curing abdominal pain.

It is admitted that the removal of the cause of pain in the abdominal organs is ideal, and that blocking of pain perception is only a makeshift, but a makeshift almost as good as a cure, provided the cause of the pain is not rendered more dangerous to life when not sending out the harassing pain signals.

Two great difficulties are encountered in the blocking of pain, *i.e.*, (1) finding the location of the pathways which are to be blocked, and (2) avoiding the blocking of other fibers adjacent to them, the function of which may not be known, since while in common parlance a nerve is spoken of as motor, sensory, or sympathetic, actually all nerve trunks are composed of mixtures of one or more of the three. For example, the vagus has both sympathetic and sensory fibers; also the splanchnic nerves con-

tain many sensory fibers while being composed mostly of preganglionic sympathetic fibers

It is believed now that the afferent fibers in the sympathetic nervous system are connected with the posterior root ganglia of the spinal cord and, therefore, the same as any other sensory nerves. Most sensory fibers from the upper part of the abdomen pass to the spinal cord through the splanchnic nerves and the white rami communicantes of the sixth to the ninth thoracic nerves. A de S Pereira (Tipografia Porto Medico, Porto pp 341, 1929) has shown that the splanchnic nerves may be connected also with the fourth, fifth, tenth, eleventh, and twelfth segments of the dorsal cord. Anesthesia of the visceral peritoneum and of the organs of the upper part of the abdomen is caused by blocking of the splanchnic nerves.

It is more complicated and difficult to block pain from the lower abdomen than from the upper abdomen for the following reasons. The pathways are more numerous, more intricate, and less well known, the nerve arrangement is different in different species of animals and in the 2 sexes of the same animals, in man the nervous structures are different from those of animals.

J R Learmouth (J Urol 26 13 (July) 1931) traced some forms of pain from the region of the bladder up along the sympathetic nerves. The 2 hypogastric nerves arise from the presacral nerve which is formed from fibers coming on each side from the upper 4 lumbar sympathetic ganglia and joining in front of the fifth lumbar vertebra. Learmouth traced connections between the nerves in the lower and upper parts of the abdomen by stimulating the presacral nerve and causing pain in a man in whom spinal anesthesia had produced

analgesia distal to the tenth dorsal segment. He claims that tactile and thermal sensations pass out of the pelvis through nerves which come from the sacral part of the spinal cord.

J Morley ("Abdominal Pain," E and S Livingstone, Edinburgh, 1931) describes a type of pain which is felt in the shoulder during an attack of *gallstone colic* or *subdiaphragmatic inflammation*, carried by the few sensory fibers in the phrenic nerves. Occasionally it is necessary to cut the phrenic nerve to relieve this pain.

Pain can leave the abdomen by still other routes, *ie*, the aortic plexuses and then through the rami communicantes to the upper dorsal spinal cord, or by the ganglionated sympathetic chain. These sensory paths are not very important or it would be more common to encounter abdominal pain in subjects whose upper dorsal cord is severed.

There are so many connections between the central plexuses and the ganglionated chain in the abdominal sympathetic nerves that it would be impossible for them all to be surgically destroyed. This is unnecessary, however, because the vast preponderance of the sensory fibers from the upper part of the abdomen pass into the greater splanchnic nerves which go directly to the spinal cord with very little dispersion in the ganglionated chain.

One great difficulty in blocking the pathways of pain lies in the lack of complete and accurate knowledge, in great detail, of the number of sensory paths and their variations; thus, in the study of the pain pathways from the heart it has been found that there are 8 paths from the heart to the ganglionated chain, and from the ganglionated chain there are numerous paths to the spinal cord and brain. With so many

avenues of pain transmission from the abdomen the difficulties to be encountered in the accurate placing of the syringe needle for novocaine or alcohol, or the scalpel will be readily appreciated.

To these difficulties comes evidence to show that even the anterior roots of the spinal cord contain sensory fibers, necessitating their cutting along with the posterior roots to relieve pain from neuromas or carcinomatous metastasis, for while the pain stimuli usually travel through the posterior roots, when those paths are destroyed their function is taken up by the anterior roots in many cases.

G. Piéri (Presse méd 36:1173 (Sept 15) 1928) avoids the difficulty by removing part of the ganglionated cord, but in so doing destroys many fibers which compose the greater splanchnic nerve. The advantage of section of one or more posterior roots lies in the preservation of the sympathetic fibers leading to the abdomen, there are 2 disadvantages however (1) sensation is lost in the corresponding dermatomes, and (2) pain is often persistent after the operation.

Various procedures to block the pain of tabetic crises have failed, because of the location of the origin of the pain within the cord.

W. J. Mixter and J. C. White (Arch Neurol and Psychiat 25 986 (May) 1931) reported **unilateral splanchnicotomy** with good results. Many animals which have had both major splanchnic nerves cut suffer from diarrhea, emaciate and go into increasing debility if they survive the operation, which has for them an immediate high mortality.

S. G. Baxter (Ann J Physiol. 96 349 (Feb) 1931) tested the pancreatic juice of rabbits after destroying their

splanchnic nerves. He found the strength of the pancreatic enzyme greatly reduced after the operation.

J. R. Learmouth (*loc cit*) reports that, in men, **lumbar sympathectomy** or section of the presacral nerve does not affect potency or ability to have orgasm, but it does interfere with ejaculation.

W. C. Alvarez (*loc cit*) concludes his article on "Abdominal Pain" with a summary of the difficulties in the way of further research. He states that several difficulties exist in the way of devising and testing operations for the relief of patients with intractable abdominal pain. To begin with, the work, in order to be convincing, must be done by conservatively minded men who will not become too enthusiastic over a few, perhaps temporary and apparently good results, and who will select cases with care. The patients will first have to be studied thoroughly, so that when clinicians finally read the reports of the work, they will not be saying, "Why that woman should never have had a nerve section, she should have had her gall-bladder removed, or she should have been given a test cure." Few observers realize that in many cases any operation is likely to give relief for from 3 to 9 months.

In the last few years Alvarez has seen many patients who might well have profited from the resection of sensory nerves, but in most instances he refrained from suggesting any attempt along this line because the individual was neurotic, psychopathic, or constitutionally inadequate, and, therefore, a poor subject for surgery. In other cases, especially in which migraine was a factor in the disease, Alvarez was not sure that relief of abdominal pain would work a cure.



In order to learn something definite about the value of nerve blocking, one would like to work with patients who are cooperative and intelligent, who will stop complaining when the pain ceases, who are ready to accept the risks of experiment, and who will not be annoying or vindictive if the operation does not do all that they hope it will do, or if it leaves them with annoying analgesia or paresthesia.

In many cases it is difficult to ascertain where the nerve blocking or sectioning should be done, and in others, the patient, after submitting to one or more somewhat painful and nerve-racking paravertebral injections, may refuse to go on with the study. It may be that nerve section would bring relief to some of those persons who now suffer with intractable duodenal and especially gastrojejunal ulcer, but for many of them it could hardly be advised because of the danger of silent perforation into the colon or other neighboring organ.

In expert hands rhizotomy does not carry much surgical risk, and the preliminary laminectomy does not seem to weaken the spine.

More histologic studies should be made on abdominal nerves and ganglia removed after death or during operations on patients with unexplained abdominal pain and the surgeon and the pathologist should keep a better watch for disease of these structures. Scarring lesions have been found in the sympathetic ganglia, lesions which might easily give rise to pain. The large sympathetic ganglioneuromas do not ordinarily cause pain, but those of von Recklinghausen's disease occasionally do. As Wohlwill says, the discouraging feature is that serious degenerative changes can be found in the sympathetic nerves of patients who died uninterest-

ingly of well-known diseases, while nothing wrong can be found in ganglia removed for the relief of severe neuralgia, asthma, or angina.

Most of the patients with unexplained abdominal pain are not sick enough to require or to accept nerve blocking measures, but some of them are incapacitated, and the time has come when the gastroenterologist should at least be aware of the fact that the neurosurgeon might be able to help him. As Grant has pointed out, when the neurosurgeon can be of assistance, he ought to be given an opportunity to see the patient before the latter has become so demoralized that nothing curative can be tried.

#### ABDOMINAL SURGERY.— PRINCIPLES AND TECHNIC.—

According to D. P. D. Wilkie (Lancet 2:803 (Oct 16) 1929), the fundamental law of operative surgery is *gentleness*. Its observance is particularly important in operations on the abdomen. Traction and tension must be avoided. The normal state of the abdomen and its contents is one of relaxation. When disease or operative measures interfere with this relaxation and introduce tension, pain results. In any major abdominal operation, *adequate exposure* is of prime importance in order that lesions may not be overlooked. A second cardinal necessity is *effective mobilization*. Immobile organs must be mobilized by strategy based on anatomical facts rather than by force. This is demonstrated in resections of the colon, duodenum, and appendix, and particularly in removal of the spleen. In the mobilization of these organs there are 2 structures to be divided: (1) the peritoneal folds which retain them, and (2) the thickened extraperitoneal cellular tissue known as the fascia propria. The

division of the extraperitoneal fascial bands helps most in the immobilization process

In resections of the gastrointestinal tract, leakage from a suture line is usually due to *tension* resulting from inadequate mobilization. For safe anastomosis the layers must be sutured together without undue tension. The ideal method of anastomosis is the use of a single layer of interrupted Lembert sutures, lightly tied so as not to interfere with the blood supply. When continuous sutures are drawn tight the margins are usually strangulated and infected sloughs and leakage result. Tension within the bowel from the retention of gas may be relieved and drainage of the lumen accomplished by **enterostomy** or **cecostomy**.

In surgery of the abdomen it is often necessary to resort to a *2-stage operation* in which the first stage is the minimal procedure, that will give relief and tide the patient over the crisis, and the second stage is the radical treatment of the causal factor. During the interval between the operations, the general condition improves and the local condition in the vicinity of the lesion may be restored to normal.

*Multiple pathological lesions* are frequent in the abdomen and the surgeon should search for them unless the operation is of an emergency character. In order to avoid missing pathological lesions adequate anesthesia and a generous exposure are essential. It is important to make a record of negative findings for future reference.

Most *abdominal pain*, excluding that due to irritation of the parietal peritoneum, results from spasm of, or tension in the hollow viscera. No form of intraabdominal tension is more important than that of the acutely ob-

structed appendix. Two distinct pathological processes occur in the appendix *viz.*, acute infection of the wall and acute obstruction of the lumen. In the former, the temperature rises, but in the latter, fever is absent during the early phase, when diagnosis is most important. Ninety per cent of the deaths from acute *appendicitis* occur in cases of primary obstruction of the appendix with resultant tension, gangrene and perforation. The rising death rate could be checked if appendicitis were more generally recognized as a type of acute intestinal obstruction demanding immediate operation.

**Technic.**—Specific local immunity can be produced by introducing any foreign material, bacterial or otherwise, into the peritoneal cavity several days prior to the operation or by opening the abdomen and handling of the viscera before the operation. In cases of **resection of the colon** the administration of *2 preliminary injections of streptomycin and bacillus coli vaccine* prior to operation results in a definite increase in resistance to peritoneal infection.

The **Mikulicz-Paul 2-stage operation** and its modifications are valuable methods of treating *obstructing growths in the colon*, especially in feeble patients.

In *intestinal obstruction*, **drainage** of the obstructed gut will afford some relief, yet death may occur even when drainage is free. The replenishment of body fluids to combat dehydration is the first indication in the treatment. Hypertonic salt solution is of special benefit. It is of importance to remember that fluid in an obstructed bowel is toxic, but if the same fluid is introduced into the normal bowel below the obstruction it may be life-saving. The physiological lack of intestinal secretion below the obstruction combined with a patho-



logical retention above it is a problem which should receive further study

In *acute diffuse suppurative peritonitis*, **drainage** is helpful if it relieves tension by releasing purulent exudate. If the tension is due to intestinal distention rather than a peritoneal exudate, an **enterostomy** or **cecostomy** will be indicated rather than peritoneal drainage, as it not only permits the release of gas, but also acts as an inlet for fluid to combat dehydration

**INCISIONS.**—F W Bancroft (Arch Surg 21 289 (Aug) 1930) points out that incisions for abdominal exposure should be planned to avoid trauma to nerves. The tendency has been to attempt to follow muscle planes and frequently to sacrifice nerves, although it is known that in the absence of infection, muscles heal well

The author believes that, whenever possible, *incision through the right rectus muscle should be avoided*. If the surgeon prefers an incision to the right of the median line for exploration or for better approach to the appendix, the *Kammerer modification* is preferable to the usual right rectus incision. When the rectus is drawn to the mesial side the nerves can be easily identified and retracted up and down so as to allow satisfactory exposure, and if sacrifice of a nerve is necessary, it can be done under the eye, without unnecessary ligation. Moreover, in this type of incision deep epigastric vessels are not encountered; therefore, there is less bleeding

*Upper or lower paramedian incisions* are satisfactory because they do not encounter vessels or nerves of much importance

The *McBurney* and the *low Pfannenstiel incision* are ideally planned to avoid trauma to the nerves. The *Kocher incision* for exposure of the

gall-bladder is associated with the risk of injuring nerves, but the danger is less than that associated with the right rectus incision

*Transverse abdominal incisions* extending either to or through the rectus muscles encounter fewer nerves than lateral vertical incisions

J Souza Mendes (Rev sud-am de méd et de chir 2 45 (Jan) 1931) advocates a method consisting in a direct inspection of the peritoneal cavity through an incision not more than 2 cm in length, with the aid of a Killian's nasal speculum and a head-lamp. A long pair of Hartmann's forceps is employed to push aside coils of intestine which impede a view of the region inspected. It is claimed that this procedure can be conducted with the aid of **novocaine anesthesia** alone. The method is recommended in particular for the following conditions: (1) in cases of abdominal contusion where rupture of gut is suspected, (2) in perforating wounds of the abdominal wall, the wound itself providing an opening for inspection, (3) where it is desirable to make a certain decision about the site and extent of tumors before a major operation, and sometimes for the removal of biopsy specimens, or of fluid from cystic tumors, when transabdominal puncture is difficult or dangerous; (4) in cases of chronic peritonitis to facilitate direct inspection of characteristic tuberculous or neoplastic lesions; and (5) in certain cases where direct inspection of the stomach, duodenum, or gall-bladder is a valuable preliminary to ordinary laparotomy

J L Yates and Forrester Raine (Surg Gynec Obst 52 1020 (May) 1931) conclude that *simple incisions* that provide adequate exposure for the majority of intraabdominal operations

which can be closed soundly, heal rapidly, assure an early recovery of usual activities, and obviate subsequent complications, must be adapted to conform with the structure, function, blood and nerve supply of the parietal tissues.

*Median, paramedian and gridiron incisions* can usually be so utilized as to fulfill these requirements, provided the relaxation provided by anesthesia suffices to prevent forceful muscular contractions during the operation, and the closure obtained does not impair healing, is sound enough to prevent early disruption of the wound or ultimate stretching that leads to diastasis and to hernia.

**POST-OPERATIVE COMPLICATIONS.—Adhesions.**—A H Curtis (J A M A 94 1221 (Apr 19) 1930) makes a thorough exploration of the entire peritoneal cavity in all cases in which the abdomen is opened. During the past 3 years he has often found "violin string" adhesions between the anterior surface of the liver and the anterior abdominal wall and has been impressed with the frequency of co-existing gonorrheal disease of the Fallopian tubes in these cases.

He states that patients with such adhesions are often thought to have diaphragmatic pleurisy, colitis, or gall-bladder disease. During the past 2 years he has seen more than a dozen patients with adhesions of this type. He believes that gonorrheal disease is not so frequently limited to the pelvis as has been assumed heretofore, and that the possibility of adhesions between the liver and abdominal wall should be considered in the cases of female patients presenting symptoms of gall-bladder disease or pleurisy.

F. W. Bancroft (Arch Surg 21.289 (Aug) 1930) believes that injury to

nerves, when making abdominal incisions, with subsequent neuroma formation or neuritis, occurs frequently, and that such injuries are often diagnosed as *post-operative adhesions*. The injuries are probably often caused by ligation of nerves with blood-vessels.

The diagnosis of neuroma may be made by testing out the sensory distribution of the nerve and by temporarily blocking the nerve by injecting procaine hydrochloride.

**Foreign Bodies Left in During Operation.**—I Grunstein (Zentralbl. f Gynak 54 2839 (Nov 8) 1930) points out that during operation foreign bodies are occasionally left behind. Various methods have been recommended to prevent gauze compresses from being left behind, or if they have been overlooked, to make them detectable by x-ray, *viz.*, attaching a metal ring, bronze wire or a leaden weight to each compress. However, all these procedures have their disadvantages. Cahn had the idea of preparing a special gauze for use in operations. Threads, impregnated with thorium hydroxide, are woven into the gauze. These threads produce a shadow in the roentgenogram, especially when they are massed together as in the case of a compress. The so-called contrast gauze may be washed, sterilized, soaked with iodoform or other substances, or retained for a time in a body cavity, without losing the quality of being impermeable for x-rays. It has no irritative effects.

**Pleuropulmonary Complications.**—E Debenedetti (Arch. ital. di chir. 26 541, 1930) discusses the pulmonary complications of abdominal disease other than frank suppurations. He refers especially to diseases of the structures of the upper part of the abdomen. The functional complications include cough

and dyspnea, and the anatomical complications, pulmonary congestion, bronchitis, pleurisy, atelectasis, and massive collapse of the lung. Several cases are reported.

A study of the pathogenesis of these complications requires a consideration of the anatomical connection between the abdominal and thoracic organs by way of the blood, lymph, and nervous systems, especially the vegetative nervous system.

Complications of an *infectious* nature are well explained on the basis of extension through the blood and lymph streams. It is noted that such complications occur more frequently after operations on the peripheral structures of the body which drain through the systemic venous system directly to the lungs than after operations on parts of the abdomen which drain through the portal system. However, lung infection may be favored also by reflex impairment of pulmonary mobility, circulation and elastic tone.

*Noninfectious* complications are the result of changes within the lung caused by reflexes through the vegetative nervous system. The author discusses the close connection of the upper abdominal organs and the lungs through this system.

The mechanism of the development of noninfectious pulmonary complications from abdominal conditions lies principally in disturbances of vasomotor and bronchomotor tone. The degree of change is directly proportional to the intensity of the afferent stimulus. Certain pulmonary complications may be produced experimentally by the production of visceral reflexes.

*Post-operative* complications in the lung may be the result of stimulation of the splanchnics by the trauma of opera-

tion. The rich distribution of the nerves in the upper abdomen accounts for the greater incidence of complications following operations in this region than in other regions. Although the anesthetic may play a rôle, the principal problem for the future is the reduction of surgical trauma.

It is shown by references to the literature and by personally collected figures, that *thrombosis* and *embolism*, and *massive collapse* and *inflammatory disorders of the lung bases*, are more likely to be encountered after abdominal operations than after surgical procedures in other parts of the body. Acting on the theory that this special liability depends in some way on an interference with respiratory function, a study has been made by D. H. Patey (Brit. J. Surg. 17:487 (Jan.) 1930) of the effect of an abdominal operation on the mechanism of respiration. It is concluded that any influence that interference with respiration has is of a predisposing nature only, and that other factors are also necessary for the development of these complications.

C. J. Fuller (Lancet 1:115 (Jan. 18) 1930) has reviewed and classified post-operative lung complications in 1478 cases. The most frequent were *bronchopneumonia* and *bronchitis*, and the next most frequent, *infarction* and *massive collapse of the lung*. The incidence of lung complications was highest (22.6 per cent.) after operations on the upper part of the abdomen. Of the operations in this group, those performed for ruptured peptic ulcer were followed by lung complications most frequently (40 per cent. of the cases). The length of time required for the operation did not seem to have any direct relation to the incidence of pulmonary complications.

**Ulcer of Abdominal Wall.**—F S Lynn (J A M A 97 1597 (Nov 28) 1931), in searching literature dealing with postoperative gangrenous ulcer of the abdominal wall, collected 21 cases. Of these, 15 have occurred in males and 14 have followed operations for appendicular abscess or peritonitis. Ten patients have been above the age of 45 years.

**Etiology.**—No specific factor in producing these gangrenous ulcers has as yet been found. The author draws attention to the investigation of Meleny, who drew the conclusion that a symbiotic function or a combination of functions of the streptococcus and staphylococcus aureus may be necessary for the production of gangrenous ulcers.

The lesion usually begins in a stitch hole a number of days following an operation and spreads slowly and indefinitely, causing marked induration of the skin, which is at first red, then livid, and finally gangrenous. The process is accompanied by intense pain, and tenderness and moderate fever, and may last for weeks or months, causing great physical and nervous exhaustion and possibly resulting in death.

The infection producing these ulcers spreads not only by continuity of tissue but also by the lymphatics.

**Treatment.**—Ordinary germicides and antiseptics are of no avail in checking this condition. It is generally agreed that the **cautery** is the ideal means of combating the spread of this type of ulcer. The cautery should extend well within the healthy tissue. **Skin grafting** may be found necessary to shorten the time of healing.

**ACETONURIA.**—H Bix (Wien. klin. Wchnschr. 43 778 (June 19) 1930) reports 4 cases of cerebral hemor-

rhages with a perforation of the ventricle in which he noted acetonuria. Analyzing these cases, he proved there was a definite existence of acetonuria of cerebral origin. The glycogen deficiency of the liver seen in other forms of ketonuria cannot be the cause of this cerebral form. The author assumes the existence of a cerebral center which governs the intermediate metabolism and, if stimulated, influences the liver in such a manner that disturbances develop in the normal course of the intermediate metabolism.

Two cases of cyclic vomiting in children are reported by S Wolff (Jahrb. f. Kinderh. 130:253 (Feb.) 1931) in which he theorizes that cyclic vomiting causes changes in the organism analogous to those in conditions of starvation and of water deficiency. In such a condition an intervening fever is able to induce circulatory shock. On account of the shock, resorption of the food in the intestine is disturbed; disturbance of the intermediary carbohydrate metabolism is another consequence of shock. In turn, these disturbances aggravate the hunger and thirst, fever enhances the effect of the shock and, therefore, the disturbances of intestinal resorption and of carbohydrate metabolism grow worse. This vicious cycle brings about death.

**TREATMENT.**—In searching for a suitable drug for combating acetone bodies in the blood, which constitute the chief danger in diabetes mellitus, O. Puesko (Wien Arch. f. inn. Med. 17: 513 (June 10) 1929) experimented with sodium bisulphite because this substance unites with acetone to form an insoluble compound. To determine the toxicity, the drug was first injected in solutions in various concentration in animals; the intravenous injection of 2 c.c. (32

minims) of a 5 per cent solution of sodium bisulphite in a rabbit did not produce the slightest harmful effect. Small amounts were then injected into patients with diabetes mellitus. When injected subcutaneously there was no effect on the ketone bodies of the blood or urine, but when injected intravenously it produced a rapid transient decrease in the amount of ketone bodies in both the blood and the urine.

**ACETYLCHOLINE.**—The salts of acetylcholine, especially the hydrochloride and the hydrobromide, act as antagonists of epinephrin physiologically, according to M. Perrin and M. Kuntz (Paris *méd.* 1.494 (May 23) 1931) as proven by their experiments. The action of these salts is chiefly that of vasodilation and hypotension, affecting especially the peripheral arterioles. A series of important observations were made with reference to the influence of these salts on profuse perspiration in tuberculous persons. Perrin and Kuntz state that their findings were especially favorable, more particularly when considering the fact that the weak doses of the salts given neither produce any toxic effects nor diminish the other body secretory functions. These drugs in no way affected renal secretion, but in some instances the total amount of urine given off was increased after cessation of the perspiration. If the oral route is ineffective, the drug may be given subcutaneously. Acetylcholine is a therapeutic agent that may be recommended in combating such a distressing, debilitating and annoying symptom as perspiration in tuberculous individuals.

**ACIDOSIS.**—Broadly speaking, acidosis may be looked upon as a disorder of metabolism accompanying

many disease processes. L. Findlay (Brit. Med. J. 1.433 (Mar. 14) 1931) compares it in this respect with fever. In both, the disturbing factor, acid in one case and heat in the other, is produced under normal conditions and the disturbance is the result of the loss of equilibrium between production and loss. This recognition of accumulation of heat or acid in the body is in no way pathognomonic of any particular disease process, though there may be variations in degree and in the type in different diseases. To attempt to raise the subject of acidosis to the position of a clinical entity would be far from correct, according to the author. He believes that testing for acidosis is like taking the patient's temperature and he compares tuberculosis with diabetes, in respect to taking the temperature and determining the acetone in the urine.

In the beginning it must be appreciated that an acid state of the blood does not exist during life. The circulation of a free acid (one not combined with an equivalent amount of base) is impossible save for carbonic acid, which is the only free acid found in the blood. Of the entire amount of carbonic acid in the blood, only 5 per cent is normally present in the free state, the remainder being combined with alkali. The ratio between the free and combined acid is the determining factor in the reaction of the blood. What is understood by acidosis is a tendency to the production of a state of free acid in the blood if chemical processes were permitted to go on uncontrolled. The symptoms of the condition as well as the tests available are evidence of the means by which the body attempts to prevent such a condition.

Acid is constantly being produced in the body as a result of catabolism but

its neutralization and excretion are provided for through the activity of the blood and the excretory organs, the lungs and kidneys. When the production of acid is increased by disturbed function of the body, the efforts of the latter must be increased. If the excretory organs are in any way impaired in their function the problem of elimination becomes more difficult.

The author states that it is a fundamental law that the total acid and basic elements which go to form the reaction of the blood are practically constant and perfectly balanced with each other. The combination of abnormal acids with the ever present alkali leaves the carbonic acid, a more volatile one, free in the circulating blood, which has a low carbon dioxide combining power as a result. This carbonic acid stimulates the respiratory center to greater activity with the resulting symptoms of hyperpnea. In some instances, the author points out, the low carbon dioxide content of the blood does not always indicate a tendency to the production of a more acid state of the blood. If there is a more rapid loss of carbon dioxide than usual, for example by forced respirations, especially seen in high altitudes, the tendency will be toward the production of a more alkaline blood and the state or condition of alkalosis is said to exist. In these conditions of alkalosis, especially seen in pyloric stenosis, there is a development of acetonuria from the overproduction of organic acids of the oxybutyric series, in an effort to combat the condition of alkalosis. This is a most important finding, as it refutes the popular opinion that the presence of acetone in the urine is indicative of acidosis.

To have a clear understanding of the condition of acidosis, the author em-

phasizes the importance of a knowledge of the factors leading up to the change and these are embodied in the clinical history. This so-called "buffer action" of the blood is not the sole means of the body's protection against imbalance since the excretory functions of the lungs and kidneys, and probably intestine, also play an important part.

Many volatile acids of the oxybutyric series are thrown off by the lungs while the kidneys encourage the increased excretion of acid by the increased production of ammonia to neutralize it.

In fatal cases of *gastroenteritis* a state of acidosis is often observed. Here there is an increased production of acid and an increased loss of base available for its neutralization. The former is the result of lack of absorption of nourishment from the intestinal tract and the latter accompanies the loss of fluid seen in vomiting and diarrhea. The degree of acidosis is a measure of the severity of the gastrointestinal disturbance and fluids must be replaced at all costs to prevent the formation of acetone.

*Diabetes mellitus* is the classical disease to illustrate the formation of an acidotic condition. The body is unable to metabolize or combust sugar, so that the fats are incompletely burned with the production of ketosis. There is a competition of these acids with the carbonic acid for the combining power of the alkali reserve and the latter, being more volatile, is left free, resulting in a hyperpnea. Because of the diuresis of diabetes there is a washing out of the fixed alkali (sodium, potassium and calcium) available in the body for neutralization. The formation of ammonia by the kidney is of extreme benefit in the conservation of the fixed alkali of the body, allowing the former to combine with the abnormal acids. It is probably



this factor, *i e*, the lack of production of ammonia in severe renal disease, which accounts for the severity of diabetes mellitus in the presence of renal disorders

**ACRIFLAVINE.—UNTOWARD EFFECTS.**—C A Birch (Lancet 1: 269 (Jan 31) 1931) finds that an acute toxic hepatitis may occasionally follow the intravenous use of acriflavine, and he describes 3 cases of jaundice in a series of 100 cases of gonorrhea treated intravenously by a 1 per cent solution of acriflavine with the use of 10 c c (2½ drams) 3 times weekly. The jaundice appeared, as a rule, between 3 and 4 months after the last injection, and lasted for from 4 to 6 days. Occasionally, icterus of the skin may appear soon after the intravenous injection of acriflavine, but this is merely transitory and not due to hyperbilirubinemia.

**THERAPY.**—D S Thurber (Canad M A J 23 665 (Nov) 1930) studied the effects of acriflavine hydrochloride in 7 cases of undulant fever, the drug being given intravenously. Seven other patients with the same disease were used as controls. In 5 cases in whom the drug was given, the fever was controlled within the first 4 weeks, while in 2 the fever continued but at a diminished level. In the 7 control and untreated cases, the disease lasted from 9 to 24 months, and 2 of the patients died.

The best results were secured in the patients treated in the earlier weeks of the affection and before the development of joint symptoms. If arthritis has appeared, acriflavine hydrochloride appears to have no effect therapeutically. Of the drug, 0.1 to 0.3 Gm (1½ to 5 grains) should be dissolved in 20 c c (5 drams) of warm normal saline

immediately before injection. At the time of injection, after proper venipuncture has been obtained, the drug in solution is added to about 200 c c (6¾ ounces) of warm salt solution. The dosage of acriflavine varies according to the age of the patient and his condition, and the number of previous doses given. It should be given slowly (approximately 5 c c—80 minims—per minute) to avoid unpleasant symptoms.

After the injections a decline, a rise, and a final decline in the fever is observed. Thurber encourages the use of acriflavine in cases of undulant fever in which arthritis has not as yet appeared.

**Psoriasis vulgaris** has been treated successfully by the intravenous use of acriflavine. S E Sweitzer and P K Allen (Minnesota Med 13 818 (Nov) 1930) studied 20 cases in which it had been tried, and all but 3 of these patients showed prompt improvement; in 4, the results were especially good. These observers point out that the use of actinic rays undoubtedly assists the value of treatment with acriflavine. Three of the patients treated, however, showed no improvement with the drug, nor showed any benefit from the addition of actinic therapy. The authors advise that 0.1 Gm (1½ grains) of the salt be dissolved in 20 c c (5 drams) of sterile distilled water, and slowly injected into the veins 3 times a week. When the treatment has been effectual, a gradual flattening of the papules and a diminution of the scales and appearance of pigmented areas is the rule. The latter fade slowly and are the last of the signs to disappear.

**ACROMEGALY.**—The case of a woman, aged 52 years, is reported by E Martin (Revue méd de la Suisse Rom. 49 639 (Sept 25) 1929) who

developed symptoms of acromegaly after an operation for an adenomatous goiter. X-ray examination revealed an enlargement in the sella turcica. A persistent bitemporal hemianopsia was not relieved by anything until a hypophysectomy was accomplished by the nasal route 3 years after the thyroidectomy. Her vision returned to normal and the size of the hands and feet diminished somewhat. Menses returned and she remained well for the next 3 years. Following this, polydipsia and polyuria coincident with a loss of weight occurred with hyperglycemia and glycosuria. Acetone and diacetic acid were also present in the urine. With the use of insulin and a strict diet the *diabetes* was controlled. The observer concludes that there exists a relationship between the nervous system and the glands of internal secretion especially the thyroid, hypophysis and suprarenals and carbohydrate metabolism. He believes there is a histophysiological relation between the glands of internal secretion and the sympathetic nervous system.

Another case is reported by E. P. Ralli (Arch Int Med 47:329 (Feb.) 1931) demonstrating acromegaly with severe diabetes and xanthoma diabetorum. The acromegaly occurred in adolescence and the diabetes followed it. There was considerable difficulty in keeping the patient sugar-free even with large doses of insulin, no doubt as a result of pituitary hyperactivity. There was in this case little doubt of the fact that it was a true case of diabetes mellitus, as evidenced by the xanthoma, hypercholesteremia and hyperglycemic curves.

An individual, aged 27 years, having symptoms of acromegaly over a period of years is reported by Carnot and Bouttier (Rev. méd. de la Suisse Rom.

49:392 (Sept. 25) 1929). This patient exhibited an increase in the size of the hands, feet, severe pains and increasing size of the maxillae, lingual hypertrophy, enlargement of the sella turcica and thickening of the cranial bones. Menses were irregular but there was a persistent lactic secretion from the breasts. Injection of urine from this patient had no effect upon the development of activities of the genitalia or hormones of hypophyseal origin. This author demonstrates the 2 component parts of the pituitary lobe and its secretion. He points out the fact that the anterior lobe hormones stimulate mammary secretion, while the posterior lobe stimulates activity of the genitourinary tract.

**ADDISON'S DISEASE.** I. G. Rowntree, C. H. Greene, W. W. Swingle and J. J. Pfiffner (J. A. M. A. 96:231 (Jan. 24) 1931) report observations made on 115 cases during the past 20 years at The Mayo Clinic. Every patient was subjected to the closest observation in an attempt to improve the substitution therapy. The fact that the cortical tissue of the adrenal glands is essential to life has given considerable impetus to this work. The factors which must be taken into consideration in the treatment of Addison's disease, as explained by the authors, are (1) the nature of the underlying disease and its treatment; (2) the natural cause of the disease; (3) the general care of the patient; (4) the treatment of the symptoms and complications, and (5) the results of specific organotherapy.

Fifty-seven patients were treated at the clinic by the administration of epinephrin through every body channel and cortical adrenal substance by mouth to the point of tolerance. Thirty-two cases were temporarily benefited,



while in 20 of these cases immediate results were excellent. The period of improvement varied from a few weeks to 7 years. Twenty cases were not benefited and one-sixth of the total number are living after 3 years.

During the past 5 years various other products of adrenal substance have been tried in the treatment of Addison's disease. Even ephedrin introduced into medicine by Chen and Schmidt had no beneficial effect. Szent-Gyorgyi and Koehler both worked on isomers of glycuronic acid and other extracts from the cortex of the adrenal, but to little avail.

In March, 1930, Swingle and Pfiffner announced the preparation of an aqueous extract of the suprarenal cortex which would indefinitely maintain the life of bilaterally suprarenalectomized cats. Following this they were able to revive comatose animals on the verge of death from suprarenal insufficiency. Daily injections aided in keeping these animals in good health.

In 5 cases Rowntree and Greene have been convinced of the efficacy of this product. As a result of its ability to remove anorexia, increase the appetite and weight, and produce a sense of euphoria in the patient the authors were gratified.

This cortical hormone is as yet not upon the pharmaceutical market and efforts are being made to present it to the Council on Pharmacy and Chemistry of the American Medical Association in an accurately standardized form, the therapeutic value of which may be determined beyond all doubt.

Three forms of treatment are of importance in this disease. (1) the relief of dehydration during the crisis by the administration of glucose 10 per cent and sodium chloride 1 per cent, (2)

the Muirhead treatment of adrenalin pushed to tolerance plus suprarenal cortex by mouth, and (3) the administration of the cortical hormone which is effective in 48 to 72 hours. Only time will tell whether this treatment will sustain life over a period of years.

F. A. Hartman, A. H. Aaron and J. E. Culp (Endocrinology 14: 438 (Nov-Dec) 1930) report the efficacy of an extract of the adrenal cortex in a case of Addison's disease the patient being a man 24 years old. Twenty-four hours after admission he was given 5 cc ( $1\frac{1}{4}$  drams) of "cortin" intravenously and 30 minutes later 10 cc ( $2\frac{1}{2}$  drams) were given subcutaneously. Three and one-half hours after the first injection 3 injections of 10 cc ( $2\frac{1}{2}$  drams) each, were given at intervals of 40 and 70 minutes. Four hours later, 10 cc ( $2\frac{1}{2}$  drams) were given every hour until a total of 150 cc (5 ounces) had been given in the 24-hour period. Soon improvement was noted and the dose was reduced to 20 cc (5 drams) every 24 hours. The determination of a maintenance dose was very difficult and was accompanied by relapses, but a stabilization was effected and the patient remained symptom-free.

**ADENOIDECTOMY.**—The subject of adenoids *per se*, in spite of its obvious importance, receives very little attention due to the fact that they are usually thought of, if not spoken of synonymously, with the tonsils. However, from time to time, due to the increasing importance of operative end-results, the literature contains specific material on this subject. It should be understood that a *poor adenoidectomy can defeat the value of a good tonsillec-tomy* and in many instances has been instrumental in perpetuating symptoms

that were originally ascribed to the tonsils

Fink (Russ Oto-Laryng 23 480, 1930) performed 600 adenoidectomies and reports most favorable results. Concerning diagnosis he admits that he never used posterior rhinoscopy or pharyngoscopy, usually applying digital examination. He avoids the listing of all the well-known indications for adenoidectomy but emphasizes the importance of a few of them. As a main absolute *indication* he mentions difficult nasal breathing. He often operated also for some remote effects of hypertrophied adenoids, such as increased nervousness in children, and their mental and physical backwardness. As a frequent indication he finds an adenoid obstructing the opening of a Eustachian tube. All the patients were operated on in the dispensary. The author does not believe in the baseless fears of many otolaryngologists that adenoidectomy cases must be hospitalized on account of the great danger of postoperative hemorrhage. Neither general nor local anesthesia was employed with the exception of 3 cases, in which the children were extremely unmanageable! Two hours after the operation, if there is no bleeding, the child is discharged without even a tampon.

Among the *complications* of adenoidectomy the author enumerates elevation of temperature as the most frequent, tonsillitis, tonsillitis with a peritonsillar abscess, otitis media with a drum perforation, tuberculous meningitis, and pyrexia with a scarlatinous rash. The other pyrexia cases he relates to the so-called idiopathic pyrexias, which disappear by themselves in a period of from 3 to 10 days.

Contrary to many authorities, the author points out that adenoidectomy

should be performed even in children with enlarged bronchial lymph nodes when there is a definite indication for it (oral breathing with a predisposition to tuberculosis, etc.). Among the other hazards of adenoidectomy Fink mentions torticollis (3 cases, all the patients recovered) and hemorrhage (8 cases, all were so slight that tamponade was unnecessary).

In the 6000 adenoidectomies 2 deaths occurred (due to generalized tuberculous process). The author stresses that the only aim of adenoidectomy is the establishment of normal nasal breathing, which has so much to do with the future of the child.

**TECHNIC** R. F. Nelson (Arch. Otolaryng 13 834 (June) 1931) describes a technique that gives as complete *anesthesia* for adenoidectomy as has been obtained in tonsillectomy. The pharynx is anesthetized as for tonsillectomy. With a curved metal applicator, the nasopharynx is swabbed transorally with **cocaine** in the strength preferred. The inferior turbinate is shrunk and lightly anesthetized, and the choanal vault and lateral nasal wall behind the middle turbinate and below the *sphenopalatine ganglion* is well anesthetized by topical applications. With good light, the nasopharynx can now be observed through each choana, and the adenoid mass seen hanging below its vault. (Incidentally, in children this visibility of the adenoid after nasal shrinkage is often a great aid, especially in examining for recurrent adenoid, when the gag reflex makes posterior rhinoscopy impossible). With a 22 gauge, 4 inch (10.16 cm.), straight Luer needle and a 2 c.c. Luer syringe, 1 or 2 c.c. (16 or 32 minims) of 1 per cent **procaine hydrochloride** can now be injected beneath the adenoid on each

side, the needle being inserted just behind the upper rim of the choana, and the point advanced about 1.5 cm as the solution is slowly injected. In 5 minutes, adenoidectomy can be performed and digital exploration done as thoroughly and as painlessly as under general anesthesia. A **postnasal pack** or string sponge may be applied for 10 minutes if desired.

This technic is not feasible with a low deviation of the septum, unless resection of the submucous membrane is first performed, but adenoidectomy can easily accompany the latter operation. Adenoid masses confined to the fossæ of Rosenmüller also are often not accessible.

**ADRENAL GLANDS.**—A most outstanding contribution to the subject of adrenal functions is the work of F. A. Hartman, F. R. Griffith, Jr. and W. E. Hartman (*Am J Physiol* 86:360 (Sept.) 1928). The experiments of these investigators were conducted to determine the efficiency of substitution therapy in the absence of epinephrin. Cats were used as the experimental animals and fresh beef adrenals were secured, chilled and immediately transferred to the laboratory. An aqueous extract was made from the cortex shaken with 3 volumes of water; 0.1 N acetic acid was added, and solids were removed. Next the epinephrin was removed by the use of potassium permanganate method of Folin, Cannon and Denis.

As controls in the experiments, cats were injected with Ringer's solution. The controls were observed at the same time as the experiment, to be under the influence of the same conditions. Large amounts of Ringer's solution were necessary to keep the cats alive.

Comparing the average survival of 5 or 6 days for untreated animals with 12 days for the treated animals, definite proof of the presence of the hormone was given. As progress was slow, a precipitate of the new hormone was made. A greater average duration of life was found in the use of this new precipitate. The investigators found the chances for recovery are markedly diminished by the duration of the period of asthenia and prostration before the extract is administered.

The name "*cortin*" was suggested. With this extract completely adrenalectomized cats which were injected twice daily have survived an average of 27.4 days or longer as compared with 5 to 6 days for controls.

Reporting again in 1930, F. A. Hartman, K. A. Brownell and W. E. Hartman (*Am J Physiol* 95:670 (Dec.) 1930) developed a much more refined extract containing the hormone. They found that this new substance acted as a definite specific substitute for the adrenal cortex. The adrenalectomized cats were kept alive indefinitely in good condition with it. These animals ate well, gained weight, played, fought and acted like normals. It was found that the extract lowered the blood urea when it was high and increased the resistance to infections and colds. It promoted repair of the tissues and enabled the animals to withstand surgery. The animals were allowed to pass into the last stages of adrenal insufficiency which just precedes death and were revived by the cortin. It was found not to be effective when given by mouth, but when administered subcutaneously it was possible to detect its effect within a few hours.

A case of *hypoglycemia* with a tumor of the left adrenal gland and congestion

of the pancreas and the pituitary gland was reported by H B Anderson (Am J M Sc 180 71 (July) 1930) No explanation could be advanced for the hypoglycemia but 2 pathologists described the tumor as a *carcinoma of the adrenal cortex*

A most interesting case of *paroxysmal hypertension* with an elevation of the blood-pressure from 110 mms to 200 mms in 90 seconds was reported by M F. Porter and M F Porter, Jr (Surg Gynec Obstet 50 160 (Jan) 1930) During the attack the patient's pulse dropped to 55, becoming very forcible, his color was ashen and general appearance quite ill

A diagnosis of renal tumor was made At operation a completely encapsulated tumor of the adrenal was found In 74 days after the operation the patient was still free of all attacks

The tumor was firm, smooth and elastic and felt tense like a cyst Microscopic section revealed an *alveolar adenocarcinoma* probably of the *cortex* Eight cases of paroxysmal hypertension have been reported, 6 of which were due to malignancy It is usual to find a hypofunction of the adrenal gland when invaded by neoplastic cells, but in the case of chromaffin celled tumors hyperfunction is the rule. A similar case of paroxysmal hypertension has been reported by M Labbe, P L Violle and E Azérod (Presse méd 38 553 (Apr. 23) 1930)

#### EFFECT OF IRRADIATION.—

From his own investigations and the work of others, A U Desjardins (Am J Roentgenol 19 453 (May) 1928) concluded that much of the experimental work bearing on the biologic effect of irradiation of the suprarenal glands is of doubtful value because it has often been based on unwarranted deductions.

Experiments on animals show that x-rays may cause pathologic changes in the suprarenal gland, but strong dose well beyond the therapeutic range must be used to induce these changes The pathologic alterations affect chiefly the cortical portion of the gland, medullary changes may also occur, but this portion of the organ is distinctly less susceptible to irradiation than the cortex In spite of the morphologic disturbances of the suprarenals produced by irradiation under experimental conditions, the health of the animals was not impaired Since the suprarenal factor influencing blood-pressure is chiefly a product of the medullary cells, the ground for the contention that irradiation may diminish the blood-pressure in hypertension is not solid

#### IN CONGENITAL SYPHILIS.

—A most interesting series of 250 cases of congenital syphilis were examined by G L Fite (Bull. Johns Hopkins Hospital 48.1 (Jan.) 1931). He was particularly interested in the adrenal glands and found abnormalities present in 40 cases, many of which showed changes attributable to syphilis. About half of the cases were stillborn infants. Most of the other subjects had died during the first month or 2 of life, while the oldest had died at 7 months. In none of the 250 cases nor some 150 others which defied microscopic examination by poor preservation, were any macroscopic gummæ of the glands seen

#### AGRANULOCYTHEMIA.—

C. V. Richards (Arch. Int. Med. 48: 793 (Nov.) (pt. 1) 1931) presents complete anti- and post- mortem records of a case of agranulocytomia. On March 16, 1929, the patient was taken to the hospital in an ambulance; upon arrival there her temperature was 104° F.

(40° C); she breathed with difficulty, which was less when the head was elevated. Breath was extremely foul. The usual breathing was obstructed by congested mucous membrane. The pharynx and tonsils were swollen. The tongue was swollen and coated. The gums were swollen, ulcerated at the gingival margins, and were coated with a grey exudate. The tonsillar lymph nodes were swollen, firm, and extremely tender and painful. The muscles of the left thigh and right calf were very tender on pressure. The blood culture showed no growth. The white blood count was 2100.

**CASE HISTORY.**—The history of the present illness up to the time of admission to the hospital was as follows. On March 8, 1929, 8 days prior to her admission, the patient was confined to bed with acute bronchitis and acute sinusitis, accompanied by generalized aching and sweating. She apparently responded to the usual remedies. On March 11, the right maxillary sinus was drained. Severe swelling of the face on March 12, was followed by improvement on March 13. The next day the patient was extremely weak, a bright red line extended above and below, along the gingival border. On March 15 the temperature was 106° F (41.1° C), the mucous membrane of the throat was highly injected, and the cervical glands were tender and enlarged. The area of the gall-bladder and the calf of the right leg were tender. The spleen was impalpable and jaundice was absent.

**PAST HISTORY.**—The past medical history was as follows. Influenza, pertussis, measles, chicken pox, and intermittent fever, with an abscess under the chin. The patient had been subject to tonsillitis. In 1916 the lungs were

supposed to be tuberculous, and she spent 1 year in a sanatorium. The sputum was negative. She suffered an attack of hemoptysis. In 1926 a tonsillectomy was performed. The patient complained that she had tired generally for years, on exercise and at other times she had been faint, dizzy and short of breath, the pulse had been rapid. Once she had had night sweats for 1 month, and had usually felt sleepy; she had had anorexia and an occasional feeling of fulness, but no constipation, gaseous or acid eructations, nor jaundice. Menses started at 13 years, were irregular the first year, thereafter regular, lasted only 1 or 2 days, without pain.

An examination of the patient, apparently 1 year prior to her fatal illness, showed the following. A woman of short stature, whose walk and dress were quasi-masculine. There was mild hypertrichosis; the facial bones were large, hearing was diminished to 15 in the left ear by air and bone conduction; the mouth, teeth and gums were normal. The right chest showed increased tactile fremitus, higher percussion note, increased breath sounds and transmission of voice sounds; with slight lagging upon expiration; no râles were present and the trachea was not deviated. The thyroid isthmus was palpable, the heart normal. Blood-pressure, left brachial, was 130 systolic, 90 diastolic; on the right leg it was 150 systolic, 100 diastolic. The pulse rate was 84 and temperature 99° F. (37.2° C). There was normal feminine hair distribution. Pain was present on pressure of the last rib on the right, Stiller's sign (abnormal motility or flexibility of the tenth rib at the costal cartilage, found in visceroptosis) was negative. There was a scar in the region of the

appendix, and mild tenderness over the gall-bladder. The liver was not palpable. The pelvic examination was negative. The neurological examination was negative. The blood Wassermann was negative. The blood examination showed: hemoglobin 85 per cent, leukocyte count normal, 72 per cent polymorphonuclears, 17 per cent small lymphocytes, 4 per cent large lymphocytes, 6 per cent basophiles, and 1 per cent eosinophiles. Urinalysis showed albumin, no sugar, and numerous epithelial cells.

A 2 months' course of intramuscular injections of some iron preparation was received in the summer of 1926. Duodenal siphonage was also instituted, the "B" bile showing occasional bile salt crystals and group of pus cells, some mucus, and once a pure culture of *Streptococcus albus*. Cholecystitis was thought to be excluded on these findings. By Graham's method the gall-bladder functioned normally. The gastric analysis showed free acid 11, combined 8, total 19.

The impression of the patient at that time was of fatigue, gastric hypoacidity and endocrine dysfunction.

The treatment consisted of thyroid extract and increased exercise. This was (by induction) in the spring of 1928.

The diagnostic impression on March 16, 1929, upon her admission to the hospital, based upon the history of her illness prior to her admission (from March 8) and the signs and symptoms observed upon admission, were: acute sinusitis of the right maxillary antrum; Vincent's angina of the mouth and throat, and a possible septicemia.

**LABORATORY FINDINGS.**—Her course and findings subsequent to admission to the hospital, on March 16,

were as follows. On March 17, nose and throat cultures showed presence of staphylococcus, and absence of the diphtheria bacillus and Vincent's organisms, the bacillus fusiformis or spirochetæ Vincenti. The blood Wassermann reaction was negative, and the white cell count 900, with 8 per cent neutrophiles, small mononuclears 80 per cent and 12 per cent transitionals. Smears showed increased platelets, but no anisocytes, poikilocytes or parasites. The urine specific gravity was 1.025; reaction acid; no sugar; albumen present, no acetone; leukocytes and hyaline casts, of both a few.

#### COURSE AND TREATMENT.

—On March 17 her condition was essentially unchanged, but her temperature had risen 1° to 105° F. (40.5° C.). There was a slight definite superficial ulceration of the left anterior pillar, which was covered by a whitish exudate. Ten thousand units of diphtheria antitoxin was administered intravenously, and she was transfused with 500 c.c. (1 pint) of citrated blood; no reaction followed.

On March 18 the patient was weaker; the temperature rose to 106° F. (41.1° C.) and she was irrational most of the time. The same dose of diphtheria antitoxin and citrated blood was again intravenously administered, without reaction. Pulmonary edema was pronounced, and jaundice appeared. Cultures from the nose, the pharynx and the epiglottis were negative for diphtheria bacillus, but smears from the epiglottis showed the organisms of Vincent's angina. The red blood count was 4,440,000, and the hemoglobin was 70 per cent. The white blood cells numbered only 400, of which 4 per cent. were neutrophiles; 74 per cent. were small mononuclears, and 20 per cent.



transitionals; 2 per cent were not accounted for in the report

On March 19 the leukocyte count remained at 400, the patient was irrational until her death at 10 45 A M

#### POSTMORTEM FINDINGS.—

At 1 P M on March 19 an autopsy was performed, followed by the usual microscopic examination of specimens of the various tissues and culture of the heart's blood. The findings were as follows: *Streptococcus viridans* in the heart's blood culture, gangrene of the larynx and pharynx, necrosis of the right gastrocnemius muscle secondary to venous thrombosis, old tuberculous scars of the glands at the hilus of the lung, and appendectomy scar, disappearance of leukocytic elements from the bone-marrow

**TREATMENT.**—A E Taussig and P C Schnoebelen (J A M A. 97: 1757 (Dec 12) 1931) report having treated 4 cases of agranulocytosis with x-rays. The first patient received 3 treatments, of  $\frac{1}{20}$  skin unit dose each, over the long bones, and fairly large doses of desiccated hog stomach; the second patient received 3 x-ray treatments over the long bones, each  $\frac{1}{4}$  unit skin dose and large doses of liver extract. The third patient received 15 x-ray treatments over the long bones, each  $\frac{1}{20}$  skin unit dose, and the fourth patient received 10 treatments, the first  $\frac{1}{10}$  unit skin dose, the next 9 treatments were each  $\frac{1}{20}$  unit skin dose, in addition to liver extract and leukocyte extract injections. The first 2 cases recovered; the last 2 died

Taussig and Schnoebelen believe that the recovery of the 2 patients who lived was influenced by the irradiation. They question the wisdom of the  $\frac{1}{20}$  erythema dose which is usually employed, and suggest that it is too small.

**ALBUMINURIA.**—A most interesting series of observations on cases of albuminuria in persons without renal disturbances has been carried out by B Minz (Klin Wchnschr 9 2352 (Dec 13) 1930). Lack of an accurate method to determine the presence of small amounts of albumin in the urine was given by the author as an explanation for the uncertainty of the presence of this constituent of the urine of normal individuals. The instrument used was a combination of a colorimeter and a nephelometer. In testing 100 urines the author found albumin was never entirely absent. In normal individuals the amount eliminated was between 0.2 and 0.6 mg per 100 c c. If the average daily urine were 1500 c c the amount would be from 3 to 9 mg. No increase in albuminuria was detected after the consumption of large quantities of albumin (10 boiled eggs). There is a steady average or normal for this output of albumin but inflammatory conditions cause a marked increase. The author believes the increased albuminuria of hypertension is a beginning expression of nephrosclerosis and the high values in diabetes frequently concurrent with renal disorders.

R N Chopra and J P. Bose (Indian M Gaz 66 299 (June) 1931) administered opium in doses ranging from 1 to 9 Gm (15 grains to  $2\frac{1}{4}$  drams) daily in a series of 12 cases of albuminuria due to various causes. In the majority of instances the urinary output was markedly increased but in most cases there was a decided diminution in the liberation of albumin without any evidence of further damage to the kidneys. The patients' general condition improved and they all felt better symptomatically. The final conclusion of the study was that patients with marked albuminuria

may be given fairly large quantities of opium provided the bowels are kept well open

A. Fischer and H. Gehlen (*Ztschr f klin Med* 113 270 (May 23) 1930) report a case of albuminuria in which the large amount of protein eliminated consisted almost exclusively of globulin (euglobin and pseudoglobin). Neither a protein free diet nor the administration of a large amount of protein affected the composition of the protein in the urine. On the protein free diet the protein content of the blood serum, however, decreased somewhat, principally at the expense of the globulin. The chemical identification of the protein was carried out primarily by means of the tryptophan determinations. The mechanism involved in the elimination of large quantities of globulin in this case can be best explained on the basis of a secretion theory.

R. Ehstrom (*Finska lak-sallsk handl.* 73:325 (May) 1931) states that theoretically albuminuria on a neurologic basis must be considered in hypophyseal disorders with glycosuria. He describes 2 cases in which the cerebral origin for the albuminuria seems quite plausible. In both cases there developed in connection with a process in the pituitary body (indicated by changes in the sella turcica and choked disc), adiposogenital dystrophy, diabetes mellitus and albuminuria.

### ALCOHOL.—THERAPY.—

**Paravertebral Injections.**—Paravertebral injection of alcohol for the relief of cardiac pain as tried in 9 cases observed by R. L. Levy and R. L. Moore (*Arch. Int. Med.* 48 146 (July) 1931) and in 57 cases reported in the literature. Before the operator attempts this procedure, these authors advise that ex-

perience on the cadaver be acquired. Of 49 cases in which adequate data were obtained, 51 per cent of the patients experienced complete or almost complete relief, improvement was noted in 34 per cent, and in 15 per cent the operation was a complete failure. Several of the patients were only slightly or temporarily benefited, but in others the result was strikingly successful. In 1 case personally observed, complete relief from pain for 16 months was obtained. Following the paravertebral injection, many of the patients complained of hyperesthesia of the chest wall and a painful intercostal neuritis in the segmental distribution of the nerves into which injections were made. At times, this lasted for as long as 6 weeks, but it was apparently unavoidable. Fever following injection was noted in several of the patients, which fever lasted a few days. In 2 of the patients, effusion into the left pleural cavity followed the procedure.

Levy and Moore are of the opinion that paravertebral injections of alcohol offer a reasonably good hope of some relief to patients with **paroxysmal cardiac pain**. However, until more observations on a large number of patients over a longer period of time have been obtained, final judgment must be reserved. At the present it should be used only after carefully planned medical treatment has failed to alleviate the suffering. The procedure is relatively safe and so far it has been unattended by operative fatality. It is a sound physiological measure and is less dangerous than cervical sympathectomy. It should be borne in mind that the basic pathological condition is unaltered. In those individuals in whom the pain has served as a danger signal of overexertion, they should be warned against ex-



ceeding the functional capacity of the heart if relieved from attacks by paravertebral injections of alcohol

Paravertebral alcohol injections for **angina pectoris** are advocated by D. D. Pletneff (Ztschr f Kruslaufforsch 23: 177 (Mar 15) 1931), rather than the various operative procedures which have a 12 to 18 per cent immediate mortality. In order to obtain a satisfactory lasting effect, repeated injections at weekly intervals were found necessary. Pletneff advises 5 c c (80 minims) of a 1 per cent *novocaine* solution in the region of each ganglion, followed a few seconds later by 5 c c (80 minims) of 70 to 80 per cent *alcohol*. The patient is given an injection of *morphine* the preceding evening, and a dose of morphine or *pantopon* 2 hours before the injection. Except in the rare instances where the alcohol has been injected directly into the nerve ganglion, no ill effects have followed the procedure. Where the ganglion itself is injected rather than that of its tissue vicinity, an immediate attack of angina has been precipitated which attack, however, promptly passed off. Nevertheless, this observer believes that it is possible that fatal reactions may occur from some such injections improperly administered. Pletneff has obtained satisfactory permanent results in 3 of 22 cases, and fairly lasting results in many of the other cases, but only 2 showed complete failure, both of these being operated subsequently.

*Untoward Effects*—M. Molitch and G. Wilson (J A M A 97 247 (July 25) 1931) reports a case of a woman, aged 66, suffering from **angina** for 5 years, who in May, 1929, had had a left cervical sympathectomy performed, with relief of pain for 6 months. In March, 1930, a paravertebral alcoholic injection of the left upper

4 thoracic sympathetic nerves was performed, with relief which lasted for only 3 weeks, 2 months later the injection was repeated, with relief for 6 months. Eight months later, or in January, 1931, the pain returned and the patient was given another injection, following which an incomplete Brown-Séquard paralysis ensued. Although the paravertebral injection was performed on the left side, the patient revealed neurological findings that indicated a lesion on the right side of the cord, involving the crossed pyramidal tract and the spinothalamic pathway. Loss of sensation on the inner sides of both arms and hands was thought to be due to injury to the central part of the cord, thus catching the pain, heat and cold fibers as they cross. Loss of touch on the same side as pain, heat and cold, was also noted.

These observers point out that certain investigators feel that whenever touch sensation is disturbed in a Brown-Séquard paralysis, the disturbance is always on the same side as that on which pain, heat and cold is present. Molitch and Wilson (*loc cit*) are of the opinion that in this particular case, the needle entered the spinal cord itself through the intervertebral foramen. Since no alcohol was injected, rapid improvement occurred. These observers endeavored to repeat the same procedure, using a dye on 6 cadavers to determine if it is possible to enter the spinal canal, but in only 1 of the specimens was the dye found in the canal, staining the dura and a small portion of the cord.

**ALCOHOLISM.**—Studying the death rate of married and unmarried men in Bavaria, Berlin and Budapest, and of Jews and Gentiles in Prussia, Berlin and Budapest by comparative

statistics, R. Bandel (*Ztschr f Hyg u Infektionskr* 111: 256 (Apr 17) 1930) found that the greatest fall in the death rate of single men and of male Gentiles was obtained during the years in which, either because of the war or of bad economic conditions, a scarcity of alcohol existed. Married men are said to drink less than unmarried men, and that Jews, as a rule, drink less than Gentiles, and these facts, combined with the above, constitute another argument in support of the contention that the fall in the male death rate during the first few years after the Great War was a result of the decrease in consumption of alcohol. Bandel believes that there is a close relationship between the amount of alcohol used and the male death rate.

The injurious effects on health from the misuse of alcohol were studied by A. Eiselsberg (*Wien klin Wchnschr.* 43: 6 (Jan 2) 1930). He points out that there is a large number of patients who, as a result of alcoholism, are taken as patients to insane asylums; furthermore, numerous gastrointestinal disorders and other abdominal affections may be traced to the misuse of alcohol. Several cases of accidents are then described occurring among intoxicated individuals. Eiselsberg further states that 553 of 32,735 accidents were directly the result of intoxication of individuals, and he discusses the large expenditure of public money used needlessly and wasted with these accidents. This author is of the opinion that intoxication itself should be looked upon as a penal offense, rather than an extenuating circumstance, in punishment of intoxicated persons. Society should outlaw intoxication by making it a disgrace and beneath human dignity. Eiselsberg is of the opinion that physicians, especially, should take the lead in the combat against alcohol

by directing public attention to its harmful effects on health.

The effect of prohibition and all of its consequence on the health of certain parts of the community were studied by J. Hagelstam (*Acta psychiatrica et neurologica* 5: 311, 1930). Finland introduced total prohibition in June, 1919, and the following 10-year period, during which it was officially enforced, is compared with the previous 10-year period, using the data from the Maria Hospital in Helsingfors, of the medical department of which Hagelstam was the chief until July 1, 1927. In the first decade, during which the year admissions were raised from 1400 to about 2000, the proportion of cases of alcoholism never exceeded 1 per cent, whereas in the second decade, the proportion of these cases was from 6 (0.6 per cent.) in 1922, to 66 (3.3 per cent.) in 1928. Acute ethyl alcohol poisoning was relatively rare; in the 6-year period from 1914 to 1919, there were noted in the records 15 cases of acute ethyl alcohol poisoning, and as many as 41 cases of poisoning from methyl alcohol or from the use of denatured spirits, 10 terminating fatally. During the 6-year period, 1923-1928, there were 36 cases of alcoholic polyneuritis, whereas in earlier years, the few and isolated cases of polyneuritis seen could usually be traced to some infectious origin. Of the 2200 patients admitted in 1929, there were 92, or about 4 per cent, in whom excessive abuse of alcohol was noted as the cause of disease, and among these patients, 23 had more or less severe disturbance of the central nervous system (neuritis in 7 cases, epileptic convulsions in 9, and delirium in 7).

**ALCOHOLIC DELIRIUM.**—*Treatment.*—There has been an increase in the number of admissions for

acute alcoholic psychoses since the advent of prohibition in several of the large hospitals, as reported by H Goldsmith (Am J Psychiat 10 255 (Sept ) 1930), and the cases have required longer hospitalization than those of pre-prohibition days. At the Baltimore Psychopathic Hospital, during the years 1925-1927, there were 4 times as many patients admitted as during the years 1912-1914, and this condition has suggested to the author the desirability of treatment which would lessen the stay in the hospital. Spinal drainage was tried on these patients to reduce the cerebral edema, congestion and irritation, to which symptoms of alcohol poisoning are attributed. During 1928 and 1929, certain of the acute alcoholic psychoses and delirium tremens patients were treated by spinal drainage as the regular therapeutic measure, and the author states that the results were so satisfactory in the almost immediate remissions produced that it is now being advocated for use in all types of acute alcoholic psychoses. Following the patient's admission to the hospital within the first 24 hours, from 30 to 50 c c or more of spinal fluid is removed. In about 50 per cent of the cases the fluid escapes under pressure. If improvement does not follow within 48 hours, the operation is repeated. In approximately 78 per cent of the cases complete remissions occurred within 3 to 7 days. The greater majority of the cases required no special form of treatment, but some needed attention for particular symptoms. In a few of the cases of the manic-depressive class, affective reactions appeared, but were not persistent. In 78 cases, the average hospitalization period was 30 days as compared with 48 days under former methods of treatment. Ten per cent of the cases died in

acute alcoholic delirium, but in these cases, the prognosis was bad from the beginning.

The use of **strychnine** in the treatment of patients with alcoholic delirium is recommended by P Pagniez and P. Chaton (Presse méd. 39·297 (Feb. 28) 1931), who studied the effects of this drug on 42 very severe cases. Strychnine sulphate, 2 mg ( $\frac{1}{32}$  grain), was injected every 3 hours, and in some cases every 2 hours until a daily dose of from 10 to 16 mg ( $\frac{1}{6}$  to  $\frac{1}{4}$  grain) had been administered. No other medication was prescribed. The patients were required to drink **large quantities of water and tea**. When his agitation was not excessive, he was permitted to be at liberty in his room, which contained no furniture, except a draw rug. In cases of *violence*, a strait-jacket was used, but this was avoided when possible. Patients arriving at the hospital in a state of mental confusion, with hallucinations, trembling, covered with perspiration and marked insomnia, may be quieted in from 24 to 48 hours by the use of **strychnine**. After this preliminary period, the daily doses of the drug are gradually reduced. Never have the authors observed the slightest disagreeable reaction from the use of strychnine. They believe it is difficult to state the exact nature of the drug action or whether it is a specific for alcoholism or for the nervous reactions of alcoholism. However, it appears significant that in cases of delirium from nonalcoholic causes, the injections of strychnine are ineffectual.

In December, 1929, E Klemperer (Monatschr f Psychiat u Neurol. 74 163 (Dec ) 1929) described a treatment of delirium tremens with **insulin** and K. Bendixen (Tidsskr f. d. Norske Laegefor. 940 (Sept. 1) 1930) inves-

tigated the use of insulin in alcoholic delirium Klemperer states that there is an incomplete dissolution of the alcohol molecule. Intermediary products or by-products are formed which are responsible, in part at any rate, for the clinical symptoms. Since insulin was shown experimentally to hasten the dissolution of alcohol in the body, this observer was of the opinion that it would be beneficial in delirium tremens, especially because insulin has already been shown to be of value in certain disorders of the liver, an organ the functions of which are interfered with by alcohol poisoning. Klemperer stated after the use of insulin in 18 cases, that its use is without danger and is superior to the usual fractional treatment with veronal, and Bendixen's cases, similarly treated, support the conclusions of Klemperer. In 1 of the cases, the fractional use of veronal had originally been tried but without success.

**ALKALOSIS.**—D. B. Pfeiffer (Ann Surg 92:900 (Nov.) 1930) is convinced that alkalosis, although less common than acidosis, is a definite and important condition demanding clinical recognition and specific treatment. It is often to be suspected in cases of profuse and prolonged vomiting, as a result of the loss of chlorides and large amounts of fluids, in obstructive states, either mechanical or physiologic, involving the stomach and upper intestinal tract. Symptomatically it may be recognized by (1) vomiting, frequently gastric hypersecretion and dilatation, (2) dehydration with asthenia and reduced blood-pressure; (3) restlessness, irritability, nervous twitchings, sometimes typical tetany, and (4) in the later stages, stupor and coma resembling the uremia of nephritic origin. According to the

author, the urinary conditions present are those of an acute glomerulonephritis with diminution of the phenolsulphone-phthalein excretion. A study of the blood chemistry reveals a diminution of the blood chlorides and an increase in the carbon dioxide combining power. Nitrogen retention in the blood is an early and characteristic sign. The *treatment* which Pfeiffer suggests consists in restoring the chemical balance of the blood and in severe cases intravenous therapy is indicated and should accompany or, if possible, precede urgent surgery.

Of 34 cases of congenital pyloric stenosis analyzed by M. Maizels, C. B. McArthur and W. W. Payne (Lancet 1:286 (Feb. 8) 1930), 28 showed an increase in the alkali reserve at some period before operation. In no cases was acidosis present. The chlorides usually varied inversely as the bicarbonate reserve. Copious doses of physiologic solution of sodium chloride were given in all cases. Four cases showed a rise in the plasma chloride but 2 showed a definite fall in spite of the subcutaneous saline injections. The urine was alkaline and almost chloride free. Ketonuria was rare and in most cases marked improvement followed saline infusions.

**ALLERGY.**—G. Piness and H. Miller (J Allergy 1:117 (Jan.) 1930) made a study of the inhabitants of 2 towns, one a mining community with a population of 3000 and the other an industrial town of 1500. In the former, the smelter fumes, and in the latter, potash dust, were supposed to be the offending substances. The suspicion arose that the symptoms were due to *hay fever* rather than a chemical irritation. A census of the mining town

showed 132 persons suffering with hay fever, a rate of 4.4 per cent. Additional subjects for the study recruited from the surrounding countryside brought the number to 172 individuals.

A history of positive *heredity* in parents was obtained in 52 cases or about 30 per cent. The symptomatology was characteristic of hay fever and 21.6 per cent of the patients had asthma. Treatment was begun with 0.1 cc (2 minims) of a 1:50,000 pollen extract administered hypodermically and then increased in ascending doses at 5-day intervals, the final dose being 0.5 cc (8 minims) of a 1:50 extract. The total dosage was then 33,300 pollen units given in 20 injections. Because of the close control and observation kept over each group by the authors, the results were susceptible of being almost exactly evaluated. In the larger community reports on 91 patients were received. Of these 5, or 5.5 per cent, showed failure of treatment, 15, or 16.5 per cent, obtained some relief, and 71, or 78 per cent, obtained good to complete relief. In the smaller community, of the 15 patients treated, 14 were reported and all obtained practically complete relief. This was practically 100 per cent.

A view from the standpoint of *protein hypersensitiveness* of the child suffering from the so-called allergic syndromes of asthma, eczema, urticaria and hay fever is maintained by J. Ratner (J. A. M. A. 96:571 (Feb 21) 1931). He believes a carefully taken and analyzed history is a most essential factor. This should include not only the history of the typical attack in its relation to food, contact with animals, season of the year, time of occurrence and locality, but also a broad and general history of the case as a whole. In addition, a complete physical examination and laboratory tests,

including blood chemistry, cytologic studies, x-rays and 300 to 400 skin tests should be performed upon each child. He also believes that etiologic factors such as sensitization *in utero*, sensitization by passage of the antigen through the intestinal tract, and sensitization through inhalation of the antigenic dusts are of paramount importance. From an analysis of cases studied over a period of years he believes that the **elimination of offending foods or emanations**, followed by the proper **desensitization** is a sound therapeutic procedure.

The case of a woman, aged 53 years, who was subject to hives for 25 years, is reported by H. L. Alexander (J. Allergy 2:164 (Mar) 1931). The attacks followed moderate *exertion* and *overheating*. The patient's tolerance to exertion and excessive warmth was found to be low. He was subjected to immersion in a bath of rather warm water which provoked an intense urticarial eruption. The water temperature and length of immersion were gradually increased and the symptoms correspondingly diminished until the patient became tolerant to heat and exercise and experienced no further symptoms.

A. H. Rowe (J. Allergy 1:531 (Sept) 1930) insists that the allergist must study the patient complaining of seasonal hay fever from the point of view of sensitizations to other than pollen allergens. Many of these patients have *food* sensitizations which are productive of gastrointestinal symptoms, headaches, urticaria, eczema, asthma and nasal congestion. The discovery and control of such food allergies is facilitated by the use of the elimination method of diet trial.

The allergic reactivity can be counteracted, if only temporary, by the oral

administration of homogenous substances shortly before the meal, according to E Urbach (Klin Wchnschr 10: 534 (Mar 21) 1931) He terms this the **propeptone treatment**. The specificity of the allergy of the nasal mucous membrane is determined by direct local (nasal) test with diluted pollen preparations The author stresses the following advantages of the oral propeptone treatment: (1) The possibility of treatment during an attack, which eliminates the time-consuming intracutaneous preliminary treatments; (2) absolute harmlessness; (3) painlessness, and (4) the possibility of making specific diagnosis by the administration or elimination of the various propeptones

W W Duke (Am J. Surg 12:249 (May) 1931) stresses the importance of the fact that allergy is important in relation to gastrointestinal disturbances, in that they may simulate organic or functional disease due to other causes; and also, through causing edema of the tissues, muscle contraction and anomalies in secretion, can actually precipitate organic disease. The allergy of the gastrointestinal tract is naturally more commonly caused by *food* than by drugs, sera, insects and parasites. Pollen, epidermal substances, dust, smoke, volatile oils and so on, which commonly cause nasal and bronchial symptoms, are rarely absorbed in sufficient quantities to produce a reaction in the gastrointestinal tract. When this condition is properly diagnosed, the treatment is likely to be brilliantly successful

C. H Eyermann (J. Allergy 2:106 (Jan) 1931) believes that until more knowledge is forthcoming regarding migraine, and further studies are made of the type of headache induced by the ingestion of specific food, the term *al-*

*lergic headache* rather than allergic migraine be employed to describe the condition He suggests that either increased intracranial tension or cerebral edema may be the pathologic causation and that in some instances the condition may be analogous to, or a manifestation of, angioneurotic edema

**ECZEMA.**—About one-third of the cases of eczema are not relieved by the dermatologists and the pediatricians These cases often come to an allergy clinic Many of them are hypersensitive to foods and drugs

The foods which cause eczema are usually common ones, such as egg, wheat, milk It may be due to any food and is frequently caused by a sensitivity to many.

R. M Balycat (J Allergy 1:516 (Sept) 1930) reviews 181 cases, ranging in age from 1 month to 84 years and about evenly divided as to sex, coming from all walks of life

Age Incidence.	Per Cent
First decade . . . . .	26.5
Second decade . . . . .	11.1
Third decade . . . . .	14.3
Fourth decade . . . . .	16.6
Fifth decade . . . . .	14.0
Between 50 and 80 years . . . . .	17.0

History of heredity was elicited in 76.0 per cent

Biologically eczema is interchangeable with asthma, hay fever, urticaria and migraine; therefore, it is not eczema itself which is the hereditary factor.

Patients may be free of eczema for a long time while still on the same diet that excites it. Such intervals occur in other types of allergic manifestation, *i.e.*, asthma for instance. There are many predisposing and contributing factors which may precipitate an attack, constipation, nervousness, mental



fatigue, thermal and actinic factors being among them

In the 181 cases there were nearly 4000 positive reactions to skin tests. About 100 foods and 7 inhalants were responsible for these. Wheat was considered responsible in 23.2 per cent as the chief factor. Milk was the chief factor in 18.2 per cent. More than three-fourths of the cases were sensitive to inhalants, including pollen and animal dander. As was the case in migraine and urticaria, multiple sensitivity was found to be the rule.

A number of allergic eczema cases have been studied who did remain free from symptoms after focal infections were cleared away. This does not mean that sensitization to food was not the exciting factor. Many apparently innocent substances are provocative of occupational eczema, cold brine, formaldehyde, mercuric chloride, novocaine, butyn and various pastes and chemical agents.

In a large proportion of the allergic eczemas the face is involved and more often in children than in adults. In the cases here cited the face and head were involved in 82 per cent.

The author is inclined to believe that many physicians have discontinued the study of allergic eczema through misinterpretation of positive and negative tests and because the methods of eliminating positive foods from the diet were not well done.

*Treatment* consists in the thorough elimination of all foods to which the patient is specifically sensitive and other foods that experience has taught are common offenders, also the elimination of all external irritants, and desensitization of cases due to pollen.

In the majority of cases the treatment

of allergic eczema is very satisfactory. From the author's observations, he is of the opinion that one-third of the eczema cases are due to a protein sensitization as the exciting cause.

**BEE-STING.**—In a study of *allergy in its relation to bee-sting*, R. L. Benson and Herman Semenov (J. Allergy 1: 105 (Jan.) 1930) have considered the following factors.

- 1 The venom of the bee-sting
- 2 Allergic reactions in the human, caused by pollen adhering to the bee
- 3 Allergic reaction in the human from sensitization to allergens inherent in the bee.

The repeated stinging by bees appears to lead to a condition of sensitization, resulting in symptoms resembling anaphylactic shock.

The authors conclude that the presence of venom and pollen action is admitted and recognized and that they have partially succeeded through testing and treatment in demonstrating that allergy to intrinsic bee proteins exists in certain individuals and that it is amenable to specific desensitization.

**PURPURA.**—Purpura is divided into 2 groups. In one there is marked diminution of the number of blood platelets with coincident interference with blood clotting. In the other these changes do not appear. In the latter group, purpura is a symptomatic manifestation of many otherwise unrelated clinical syndromes. Among these is Henoch's purpura. This latter affection, in which there is severe abdominal cramping associated with purpura of the skin and mucous membranes, has been attributed to allergy.

F. L. Barthelme (J. Allergy 1: 170 (Jan.) 1930) cites a case in point of a woman 22 years old whose attack began with epistaxis, followed by pains in the

joints and muscles, severe abdominal cramping unaccompanied by nausea, vomiting or diarrhea, and lasting from a few minutes to 2 hours. Large purpuric spots appeared on the lower limbs, appearing in new areas every few days.

Skin tests were positive for tomato, beef, wheat and egg yolk. Abstinence from these foods relieved the symptoms. Deliberate feeding of these foods gave the following results:

Beef. No symptoms.

Tomato. No symptoms.

Wheat. Purpuric spots, muscle and joint pains, lassitude.

Egg yolk. Purpuric spots and abdominal pain.

By abstaining from wheat and egg yolk the patient remained free of symptoms for 6 weeks preceding time of reporting.

The author presents this as a case of Henoch's purpura definitely due to the allergic phenomenon.

**INFECTIOUS DISEASES OF SKIN.**—In a discussion of *allergy in infectious diseases of the skin* by M. B. Sulzberger (M. J. and Rec. 131.264 (Mar. 5) 1930), he considers the skin manifestations of allergy are perhaps the most important aids to its study, for it is the organ par excellence as the indicator of an allergic state.

The definition of allergy as the term was first applied by Von Pirquet and Schick in 1906 is the sense in which it is used in this article, *viz* "a change occurring in an organism after contact with a living or inanimate organic 'poison' and manifesting itself in an altered reaction to a second application of the same substance (or one closely related)."

Smallpox vaccination is cited as an early example, as changing the reaction of the skin (and whole organism) to a

second contact with the same virus (or one closely allied).

Tinea in its ring form, means that the process in the skin spreads toward the periphery, leaving in its wake in the center, a region of skin with a changed reaction to the fungus, an immunity to fungus infection, an allergic zone in which the fungi are rapidly destroyed. Another proof of allergy in tinea infection is the fact that after longer or shorter duration the entire skin of the patient becomes hypersensitive to trichophyton (toxins from the fungus). This reaction is allergic because through previous contact with the fungus the reaction of the skin was altered in the manner made manifest by the second contact with the same or kindred substances.

Epidermophytids of the hands, in which fungi are rarely found, are explained as being evidence of allergic areas of skin in which the fungi circulating in the blood are rapidly destroyed when they arrive through the circulation from epidermophyton infection of the feet. The hand lesions often clear up spontaneously when the feet are cured.

As nearly as can be judged, tuberculin allergy results from contact with tubercle bacilli. The reaction to tuberculin in patients with tuberculoderma divides them into 2 groups:

1 Those more sensitive than the normal.

2 Those less sensitive than normal.

In the first group the tuberculous process is usually progressive and destructive and the bacillus can be generally demonstrated (guinea-pig). In the second group the process is more benign and the bacillus usually not demonstrable. It is explained that if the violence of the second group has progressed beyond that in the first, a sort



of immunity has been acquired. Theoretically, cases capable of neutralizing strong concentrations of tuberculin should have better prospects of cure. In the case of very weak individuals the reaction does not take place, because the skin itself has lost power of reaction, not because the tuberculin has been neutralized. These 2 types of nonreaction are called respectively *positive anergy* (tuberculin neutralized) and *negative anergy* (power of reaction lost).

#### ALOPECIA.—TREATMENT.—

Sixteen cases are reported by B. Norman Bengtson (J. A. M. A. 97:1355 (Nov. 7) 1931), varying from 8 to 60 years of age in which hair was restored by pituitary gland therapy, baldness having been of 1 to 23 years' duration.

Treatment was continued for periods of 2 months to 2 years. Hair grew in white but later normal color was restored in all but one case, the oldest patient.

Dosage consisted of hypodermatic injections of anterior lobe extract, posterior lobe extract and oral administration of whole gland dried extract, from 1 to 2 c.c. (16 to 32 minims) of anterior pituitary extract 3 to 5 times weekly, posterior pituitary extract 1 c.c. (16 minims) weekly, whole pituitary 0.5 c.c. (8 minims) daily 5 days per week.

Restoration to normal weight in abnormally fat or lean patients, restoration of normal blood-pressure in hypo- or hypertension, and the restoration of normal menstruation in a case of amenorrhea were among the beneficial results noted during the treatment.

Relief of headache and rheumatic pains were also reported in addition to the stimulation of hair quantity.

The x-rays showed the sella turcica to be abnormally small in some of the cases under treatment, resulting in general symptoms of hypopituitarism. These symptoms were favorably influenced.

**ALUMINUM.**—It has repeatedly been shown by the fractional test meal that soluble alkalies like bicarbonate of soda, when given by mouth, cause an immediate and almost total neutralization of all the gastric acidity, with a temporary suspension of digestion, which phase is followed by a rapid rebound of gastric acidity resulting within a half-hour in an hyperacidity of even greater degree than in a control curve, as stated by B. B. Crohn (J. Lab. and Clin. Med. 14:610 (Apr.) 1929). Because of this dissatisfaction, a special form of the *colloidal hydroxide of aluminum* was elaborated and tried as a gastric antacid with the hope that a preparation devoid of any secondary acid-stimulating effect might be found. Crohn also points out that it seemed desirable to administer only a drug which, while reducing acidity to a point where clinical heartburn and pain were relieved, would not completely alkalize the gastric chyme and so interfere with digestion. This author found that the colloidal form of aluminum hydroxide has several advantages. It is a neutral salt, it cannot produce an alkaline reaction in a gastric chyme and is, therefore, unable to cause a paralysis of digestive function. It is an efficient antacid, which by reducing the free acidity to a minimum consistent with continued digestion, also reduces the total acidity to a point where complete cessation of subjective symptoms is almost an invariable rule. It is nonabsorbable and, therefore, nontoxic.

Crohn used this preparation of aluminum in more than 50 cases of **functional gastric secretory disturbance of the hyperacid type**, which patients complained of heartburn, belching, discomfort and constipation, cases of **gastric neurosis** and also a group consisting of **gastroduodenal ulcerations**. Relief from the use of this drug is almost immediate and may last from 30 to 60 minutes, only occasionally being followed by returns of heartburn, or the subsidence of symptoms may be complete and lasting. The pain of ulcer cases is said to cease immediately, and in the less severe cases its relief persists until the following meal. In the more severe cases, relief is just as efficient and prompt, but a later recurrence of the pain may not be prevented after sometime.

**POISONING.**—Sulphate salts of copper, nickel, cadmium, cobalt, zinc, manganese, aluminum and bivalent iron and the chloride of trivalent iron, in concentrates of 1 Gm (15 grains), dissolved in 1 liter (quart) of double-distilled water, and given under the skin into the abdomen of guinea-pigs, with constant doses of 100 mg ( $1\frac{1}{2}$  grains) per kilogram ( $2\frac{1}{5}$  pounds) of body weight, was tried by G. Bertrand and P. Serbescu (Ann de l'Inst Pasteur 47:451 (Oct) 1931) to determine the toxicity of aluminum compared with other metals. Strong doses of the drugs were lethal before complete absorption was possible. When smaller doses were given, however, the individual differences were increased and the prediction of the period of survival after injection was more difficult to determine. The order of toxicity from the more toxic to the least poisonous appears in the authors' record as follows: copper, nickel, cadmium, cobalt, zinc,

manganese, trivalent iron, aluminum and bivalent iron. Copper, nickel and aluminum showed the same differences in toxicity when rabbits were injected with doses of 100 mg ( $1\frac{1}{2}$  grains) per kilogram ( $2\frac{1}{5}$  pounds) of body weight. These results indicate that aluminum is similar to iron and is less toxic than nickel and copper when used in the manufacture of cooking utensils. These observers are of the opinion that minute quantities of aluminum introduced artificially in food are innocuous, and these quantities are in no event any greater than those found in a normal state in the tissues of plants and animals used for food.

**AMBLYOPIA.**—The term "amblyopia exanopsia" is a misnomer, according to H. M. Morton (Am. J. Ophth. 14:239 (Mar.) 1931), who attributes the amblyopia to congenital defects in structural and functional neurology, with imperfect macular or paramacular vision due to an inadequate supply or a defective function of the cone elements of the retina, with a normal number or relative increase of rod elements. He believes that amblyopia is not the consequence but the cause of disuse.

**HYSTERICAL AMBLYOPIA.** -

Two cases of hysterical amblyopia in children are reported by J. M. Robinson (Minnesota Med. 13:618 (Sept.) 1930). A girl aged 12 years complained of poor sight. Her history revealed that a month earlier she had been involved in a motor accident in which her father was killed. A boy aged 10 years suddenly became blind in one eye. History showed that his sister had recently returned from a school for the blind. Some time later vision in the right eye was normal, while with his left eye he could only count fingers at 2 feet.

No objective symptoms were found, functional tests indicated psychic disturbance and both patients recovered completely. According to a Russian writer, 4 per cent of Russian children exhibit hysterical amblyopia at one time or another. Robinson agrees that it is as common among American school children. Contraction of the visual fields and monocular diplopia are proof of hysteria. Robinson considers hysteria a "defense-reaction."

**TOXIC AMBLYOPIA.**—E. B. Dunphy (Am J Ophth 14 1048 (Oct) 1931) reports a case of toxic amblyopia in an Italian-American boy aged 13 years who gave a history of rheumatism in both knees followed by failing vision. Vision was 20/100 in each eye, with good peripheral field, but there was a central scotoma for form and color in each eye. There was a history of use of cigarettes and wine. Intra-ocular tension was normal. X-rays of the sinuses and teeth were negative. Spinal fluid was normal and the Wassermann test was negative.

The whiteness and the fluffiness of the nerve heads led Greenwood to believe that this was not a true case of toxic amblyopia. Because of the youth of the patient, Derby questioned the diagnosis of toxic amblyopia in spite of the history of alcohol and tobacco.

**AMEBIASIS.**—The late W. E. Musgrave has left a wealth of observations on amebiasis in man gathered from his many years of medical service in hospitals in the Philippines. His notes, edited by A. C. Reed (Am J Trop. Med. 11:469 (Nov) 1931) comprise a study of the protozoan parasites of the genus *Endamoeba*, which produce pathological conditions in man and which are collectively called amebiasis.

In 1875, Loesch first discovered amebæ in the stools of patients suffering with dysentery. Since that time the ameba has been proven the cause of certain varieties of colitis, and has been found to involve the liver, lung, vagina, brain, pericardium, oral cavity, bladder, appendix, abdominal parietes and is suspected of invading the blood stream.

**VARIETIES.**—There are many varieties of the ameba which are parasitic to man. Some varieties are known to be pathogenic, some are accepted as being harmless or nearly so, while many are in doubt.

The protozoologist has fairly completely established the methods of differentiation between the various species that are known to be parasitic to man, but the clinicians have not as yet been able to classify them satisfactorily, especially from the standpoint of pathogenicity.

The ameba is found to be parasitic to man throughout the world, and sporadically produces disease in all climates, but the vast majority of cases of amebic disease are found in the tropics, where they assume the same relative importance as the streptococcus in cooler climes. Countries which are backward in sanitation have a correspondingly greater amount of amebic disease.

There is probably at least a partial natural immunity to the ameba in the natives of the tropics, because very many symptom-free carriers are found, and the disease, in the natives, is relatively mild, while it is most frequent and most severe, and causes the highest mortality in adult foreigners from colder climates who live in the tropics where amebiasis is endemic. While all races, sexes, and ages are sometimes attacked, children and the aged are relatively seldom afflicted.

Tropical clinicians and sanitary engineers have traced various epidemics to infected water or foods, particularly garden vegetables, but protozoologists are of the opinion that infection usually occurs by direct infection from the infected to the uninfected, and that the eating of uncooked foods and drinking of unsafe water are relatively unimportant in the spread of amebiasis.

**ETIOLOGY.**—The epidemiology of amebiasis is indefinite, from the statistical standpoint, among orientals, because they do not require treatment except for very severe attacks, and most of the cases are diagnosed when suffering from some additional illness which has more marked symptomatology. However, W E Musgrave (*loc cit*) in selecting at random 10,000 case records from his Philippine General Hospital service, found that amebiasis was diagnosed in 1260 cases, or 12.6 per cent, and in his Medical service in St Paul's Hospital, Manila, of 5000 patients of all classes admitted during 1905 and 1906, 926 cases or 18.5 per cent, were infested with the ameba.

The native peoples living in areas where amebiasis is endemic think so little about the disease, it being so extremely common, so varied in its course and intensity, that it is impossible to collect facts upon which to base epidemiologic conclusions.

Epidemics, recognized as such, of amebiasis, are most likely to occur when a large body of unacclimated occidentals are brought to an endemic area. When the American soldiers first came to the Philippines, amebic dysentery rapidly reached epidemic proportions. Smaller epidemics have occurred since among groups of civil employees of recent occidental origin and in these epidemics many serious cases develop.

**Geographical Distribution.** Amebiasis is constantly endemic throughout the tropical belt, where it is one of the most serious sanitary problems, due to the tremendous number of cases involved. To a lesser extent this is true of the subtropical belt also. While amebiasis was first discovered in the temperate zone and exists in practically all countries, it is only sporadic in occurrence north of the subtropics. The reasons for the location of amebiasis principally in the tropics are the favorable climatic environment for the propagation of the parasite and the unsanitary living conditions and habits of the inhabitants. Musgrave, as reported by Reed (*loc cit*) asserts that an additional reason is the decreased resistance of residents of those countries, but that is untenable, as it has been shown heretofore that the natives show an increased resistance to the disease.

It is not certain what factors in the climate particularly favor the spread or increase in the severity of amebiasis, but humidity and rainfall would seem to be important factors, as the peak of infection is reached at the end of the wet season.

Change of altitude has a marked tendency to cause a severe exacerbation of symptoms in the infected, irrespective of ascent or descent, but the altitude itself does not seem to influence the incidence of the infection.

Amebiasis is much more prevalent, more severe, and the mortality is much higher among the white skinned population of the tropics than among the Malays, Chinese, Indians and Africans, to such an extent, in fact, that a partial immunity is indicated in the dark races.

The incidence of amebiasis is highest in adult life, reaching its peak at about 30 years; while affecting all ages, the

vast majority of all cases are in active adult life

Amoebiasis is 4 or 5 times more frequent in males than in females. This may be accounted for to a slight extent by the fact that males are more numerous than females in tropical countries, especially among occidentals, from whom most statistics concerning the disease arise.

**Transmissibility.**—The only sanitary conditions having a directly traceable effect upon the spread of amoebiasis are *water supply* and the supply of those *foods* which are eaten *raw*. Theories of experimenters, who claim that transmission depends almost entirely on contact with the excretions of an infected patient, or carrier, are not borne out by the apparent facts, which are that the ignorant, living in squalor, especially the children, generally escape the disease.

**Susceptibility.**—There is no evidence to show that debilitated states of general health, or the presence of other disease predisposes to amoebiasis, but on the other hand, a chronic case of amoebiasis of long standing may be altered in its course, aggravated, or cured by an acute attack of some intercurrent disease. Acute attacks of bacillary dysentery are known to have cured amoebic infection of long standing.

The amoebæ that cause amoebiasis propagate persistently in and on the intestinal mucosa and other tissues of man. Only one variety of amoebæ is generally recognized as being pathogenic, although from 1 to 3 other varieties are considered pathogenic by some authorities; they all agree, however, upon the pathogenicity of *Entamoeba histolytica*.

The incubation period of amoebiasis is extremely variable; some experimental cases have shown clinical symptoms in

a few days after infestation, while others have remained symptom-free for 11 months.

**PATHOLOGY.**—The areas of infestation in intestinal amoebiasis, in their order of frequency, are the cecum, sigmoid, rectum, ascending colon, hepatic flexure and splenic flexure; the vermiform appendix and small intestine are occasionally involved.

The ability of the *E. histolytica* to penetrate the intact intestinal mucosa, without the presence of lesions due to other causes, is generally believed.

The amoebæ are most destructive to the submucosa, through which they migrate, causing necrosis in that layer, and destroying the overlying mucosa only where they cut off its circulation by thrombus formation. Thus the intestinal wall becomes riddled with ulcers which appear to be separate, but in reality are joined under the intervening mucosa. The ulcers are elongated or oval, and their long axis is transverse to the intestinal lumen. They are usually placed on the crest of the rugæ.

The pathological lesions produced by amoebic disease are typical, irrespective of their location in the intestine, bladder, liver or elsewhere. There is an almost noninflammatory reaction between the amoeba and the invaded tissue, with very slight leukocytic infiltration. There is the production of a detritus composed of blood elements, degenerated epithelial cells and necrotic connective tissue; this is the result of a slow necrosis of selected tissues, the greater part of which is epithelial.

In pure amoebic infection of tissue, the margins of the infected area show very slight inflammatory reaction. There is very little infiltration of leukocytes, and very slight if any edema. The margins are dead-looking; there is a

great tendency to undermining and tunneling, so that the picture is one of an insidious necrosis

The infected tissue under the microscope shows clustered parenchymatous cells surrounded by an infiltration composed principally of epithelial cells. In tissue infected with both the ameba and pathologic bacteria, there may be more infiltration with leukocytes, in addition to the epithelial cells, with more redness and edema.

Amebiasis of the intestinal tract is called amebic enteritis, amebic colitis, amebic dysentery, entamebiasis and is sometimes unwisely called tropical dysentery, which is misleading in view of the prevalence of the several other important tropical diarrheas, not of amebic, but of dietary, bacterial, and unknown origin.

Amebic dysentery is the infestation of the intestinal canal by protozoa of the genus *entameba*. The disease may vary in its clinical manifestations, from complete absence of symptoms to rapidly fatal disease, characterized by severe enteritis with profound diarrhea, the development of various complications, and death from the complication or exhaustion.

**COMPLICATIONS.**—*Hemorrhage* and *perforation* of the intestine are uncommon complications of amebic enteritis, but do occur in severe ulcerations which develop gangrene.

When extension of ulceration to the serosa takes place, there may be perforation, but usually adhesions are formed between the various loops of intestine or to other neighboring organs.

In the usual uncomplicated amebic infection the onset is usually so insidious that the patient is unable to fix the time when he first started to suffer the fatigability, lassitude, slight dyspeptic symp-

toms, and dull headache that mark the early days of the disease, eventually, after perhaps many months, intermittent diarrhea, alternating with constipation, becomes marked, this diarrhea, more severe in the mornings, consists of semifluid stools without blood or mucus, and passed without pain. The diarrhea lasts a few days, during which the patient feels fairly well, but during the few days of intermission there is flatulence, abdominal distress and the general feeling after eating which the patient describes as indigestion. As this alternation of diarrhea and constipation goes on, the patient insidiously loses weight and strength, the disposition becomes irritable and despondent, loss of efficiency ensues, and, after years of gradually increasing disability, a state of chronic invalidism ensues.

Some cases of intestinal amebiasis are more acute of onset and course, with blood, mucus and tenesmus appearing a few days after the first symptoms, producing the symptom complex known as dysentery.

The diagnosis of intestinal amebiasis depends upon finding the *E. histolytica* in the stools. This is usually very easy, although even with extensive lesions, the amebæ are few and hard to find.

Secondary anemia occurs late in the disease, but the blood findings are not typical.

Fever is usually absent, except when there is a complicating abscess; and subnormal temperature is usually encountered in the advanced stages of the disease.

Pain varies in character and intensity in amebiasis, it may be caused by the amebic ulceration, or by complicating infection. Tenesmus may be very severe during acute exacerbations, especially when infection with *B. shiga* is



present Pain seems to be more severe the higher the lesions in the intestines, reaching the greatest intensity when the small intestines are involved

*Pregnancy* in a patient with amebiasis is not a contraindication to treatment, as more women will abort if untreated than if carefully treated for their amebiasis

*Malaria* associated with amebiasis is best treated with the customary use of quinine in addition to high quinine irrigations of the bowel. Quinine aids in the cure of both diseases

*Beriberi* or endemic tropical neuritis is improved by treatment of amebiasis when the two diseases coexist

*Chronic nephritis* and amebiasis are both increased in severity when associated

The most important complications of intestinal amebiasis are in the liver, thorax, appendix and urinary bladder

*Amebic abscess* formations elsewhere than in the *liver* are almost always secondary to, or extensions from, abscess in that organ *Brain* abscesses have all been diagnosed post mortem, and have been found associated with liver abscess in all cases Amebic abscess of the *spleen* is an extension of abscess of the left lobe of the liver, and abscess of the *lung* and amebic pus in the *pericardium* are extensions from liver abscess

The colon is distorted by amebic infection, with dilatations and cicatricial contractions, and in prolonged cases may lose its folds and rugæ, appearing as a straight tube

Among 100 fatal cases of amebiasis W. E. Musgrave (*loc cit*) found 26 cases of general acute *peritonitis*, 4 times from ruptured liver abscesses, 20 times from perforation in the large bowel, once from a perforated appen-

dix, and once without any perforation in a case of combined bacillary and amebic dysentery

Chronic localized adhesive peritonitis occurs to some extent in most severe cases, and is found in over 80 per cent. of the fatal cases at autopsy.

**PROPHYLAXIS.**—The individual can protect himself from amebiasis by unfailing personal hygiene, consisting of scrupulous cleansing of the hands, avoidance of unsafe water, unsafe raw vegetables, and contact with infected pets and carriers.

Community measures of prevention consist of sanitary sewage disposal, guarding of water sheds from which drinking water is obtained against contamination by human excreta, purification of the water, if necessary, and control of carriers and infected persons, all food handlers should be examined periodically to detect carriers

**TREATMENT.**—P H Manson-Bahr (Brit. M. J 1.846 (May 16) 1931) reported on the treatment of 300 cases of intestinal amebiasis, in every one of which *E histolytica* or its cysts were found in the feces, or else the typical lesions had been seen through the sigmoidoscope and the parasites demonstrated in preparations made from them Four successive methods of treatment were tried The first few cases were treated by the injection of *emetine* alone That was 11 years ago The immediate beneficial effects of the treatment were very striking, and there was an undeniable direct action on the parasite, the drug, however, would not eradicate the disease

Then 130 cases were treated with *emetine-bismuth-iodide*, in the usual doses. In 1925, having read of the favorable results obtained from *yatren* as reported in the German and Dutch

literature, Manson-Bahr administered this drug, by mouth and rectum simultaneously, to 15 cases. In the last 150 cases he combined **yatren with emetine-bismuth-iodide**, and found this combination the most satisfactory method of treatment. He cited some remarkable cases of cures in long standing disease after 12 days of radical treatment.

A drug sold in England under the name of **quinoxyl** gave similar results to yatren.

Yatren can be taken in a pill, in cachet form, or by enema. Given by mouth in large doses, yatren produced gastrointestinal disturbances, but injected by the rectum, it produced singularly little discomfort. The bowel was first cleaned out, and then the 2½ per cent solution of yatren run in by means of a rubber tube and funnel. The patient was urged to retain the solution as long as possible.

Some patients develop a raised yellow rash the day following the injection, but no other sequelæ are observed.

Yatren has a wonderful effect in healing amebic lesions in the bowel, but given by itself, relapses occur. It should, therefore, be combined with some form of emetine. Manson-Bahr prefers the emetine-bismuth-iodide preparation; he injects the 2½ per cent yatren solution into the bowel in the daytime, and administers the emetine preparation at night. Of the 150 cases treated by this method he found only 2 that relapsed, and these cleared up when the course was repeated with a stronger (5 per cent) solution of yatren instead of the usual strength, in no case did the treatment have to be discontinued on account of intolerance. Whenever possible, a sigmoidoscopic examination was made before and after treatment. The disap-

pearance of the amebic lesions had been usually recorded wherever the yatren solution had come in contact with them, and the remarkable manner in which the amebic ulcers had granulated and epithelialized had been noted. There was evidence also that yatren solution, injected into the rectum, percolated through the lumen of the large intestine. There was no evidence, however, that yatren in pill form was efficacious in eradicating infection, although Manson-Bahr believed it helped to prevent relapses.

### AMENORRHEA.—ETIOLOGY.

--There have been many recent changes in the conception of the etiology of amenorrhea. With a newer knowledge of the hormones of the ovary, the Graafian follicle has assumed an increasing importance as a factor in this condition. Interference with follicle rupture may be consequent upon a chronic ascending infection from the cervix. Retroversion may also inhibit ovulation in mature and previously active ovaries by affecting the ovarian circulation.

Follicle cysts of the ovary as a cause of amenorrhea is not infrequent. These may result from the inability of the ovum to penetrate an inflamed, thickened tunica albuginea, or may be due to an insufficient hormonal stimulation from the anterior pituitary gland, so that the follicle does not rupture. C. Mazer and A. J. Zisserman (M. J. and Rec 135 35 (Jan. 6) 1932). If the follicle cannot rupture, it becomes either atretic or cystic.

During atresia, a follicle may become distended with fluid and form one or more retention cysts. Occasionally such cysts may elaborate a sufficient quantity of female sex hormone to pro-



duce prolonged menstrual bleeding. In such cases, however, there is an absence of premenstrual endometrium, which is replaced by endometrial hyperplasia. This condition is usually due to inadequate stimulation of the ovarian follicle by the anterior pituitary gland, and requires anterior pituitary sex hormone or hypophyseal irradiation.

**Pituitary Amenorrhea.**—The pituitary gland must be considered in all forms of menstrual disturbance. A W Rowe and C H Lawrence (Publications from the Robert Dawson Evans Memorial—"Endocrine Studies," 1929), in a study of 68 women with hypofunction of the pituitary gland, found amenorrhea or oligomenorrhea (periods delayed 2 or 3 months) present in over 50 per cent.

A severe grade of pituitary failure is observed in the syndrome of adisposogenital dystrophy. The milder forms of pituitary failure are much more common and, according to most investigators, are found in 80 per cent of women suffering with amenorrhea or milder menstrual disturbances. These patients are usually stout, with much adiposity, a male type of pubic hair distribution, and with increased sugar tolerance due to the associated hypofunction of the posterior lobe. Eye-ground examination reveals contraction of the visual fields, a yellowish color of the discs, and enlarged blind spots.

The anterior pituitary gland hypertrophies after castration and the menopause. Hyperfunction is also believed to occur in amenorrhea due to primary ovarian deficiency. Mazer, in a study of 66 cases of menstrual derangements, associated with sterility, found 43 with definite evidence of pituitary malfunction.

**Ovarian Amenorrhea.**—About 20 per cent. of patients with functional

amenorrhea, are believed to have a primary ovarian hypofunction. Physically, they present a picture quite different from the pituitary type. These women are superlatively feminine in appearance, are emotional to excess, and reveal a low sugar tolerance, with an absence of eye findings. An interesting and very important finding is the presence of a demonstrable quantity of anterior pituitary sex hormone in the blood, probably compensatory in nature, and very useful in differentiating this type from the anterior pituitary type.

**Thyroid Amenorrhea.**—Amenorrhea may be due, in rare instances, to hypofunction of the thyroid. The low basal metabolic rate is not, however, diagnostic, as this may be present in a variety of disturbances of other endocrine glands. It is well-known, however, that the ovary depends on thyroid secretions to increase its chemical reactions. An interesting finding is the amenorrhea present in exophthalmic goiter, in which there is a hyperfunction of the thyroid. In this case it is the severe systemic depression which is responsible for the amenorrhea.

**TREATMENT OF AMENORRHEA.**—In properly selected cases, C Mazer advises female sex hormone therapy, either alone or combined with anterior pituitary sex hormone (prolan, follutein). Although female sex hormone has no effect on the ovaries, it does cause increased growth and vascularity of the uterus, so that the latter becomes more responsive to what little ovarian function is present or to any reactivated ovarian influence.

**AMIDOPYRINE.**—Amidopyrine, given to patients suffering from endocarditis and for the purpose of reducing fever and overcoming weakness, ano-

rexia and vertigo, was found by D Scherf (Klin Wchnschr 10 1110 (June 13) 1931) to cause gain in weight. When the amidopyrine medication was discontinued, diuresis set in and the patient began to lose weight. From this effect, Scherf proceeded to study the influence of amidopyrine on water metabolism, the drug being given to individuals with and without circulatory disturbances for 5 successive days. In 84 per cent of the patients, a water and sodium chloride concentration set in and the body weight increased. No relationship was found between the severity of the circulatory disturbance and the degree of water retention. When the medication of amidopyrine was discontinued, the retained water and salt were eliminated and the weight decreased again. In the mechanism of the water retention during and after medication with the drug, certain features of peculiar interest were noted. Amidopyrine appears to check the diuresis due to digitalis, as well as that from the use of purine bodies. So far, this investigator has not been able to decide whether the tissues are influenced directly or whether the cerebral nervous system is affected.

### ANACIDITY, GASTRIC.—

Complete gastric anacidity is rarely found, but a reduction of the gastric acidity to the trace which is ineffective in gastric digestion, occurs in about one-tenth of patients having symptoms of a kind and severity to bring them to the internist for gastric study. It is caused by, or frequently accompanies, gastric carcinoma (50 per cent), chronic gastritis, chronic tuberculosis, cachectic states generally, primary anemia, chronic diarrhea, chronic arthritis, and then there is that group which apparently is without cause and which produces no

symptoms, being detected only by routine studies. W S Pollard and A L Bloomfield (Arch Int Med 48:412 (Sept) 1931) have made particular study of a group of 25 cases of unexplained gastric anacidity, the analysis being done fractionally after hypodermic injection of histamine, 0.1 mg per 10 kilograms of bodyweight. Their conclusions were that failure to secrete acid (or indeed any actual gastric juice) occurs in a certain number of persons, apart from the well-known associations of anacidity, such as pernicious anemia and cancer of the stomach. It may be estimated that such "unexplained anacidities" are encountered in from 3 to 5 per cent of the patients in a medical clinic. In the present series the disorder was distinctly one of middle and old age, a finding which suggests that it is acquired rather than congenital, but beyond this no relation was found to age, sex, occupation, diet or habits.

It has not been possible to define any symptom-complex that is clearly associated with the gastric disorder. This point deserves especial emphasis in view of alleged "anacidity diarrheas" and other syndromes that have been described from time to time. In the present series, most of the cases were asymptomatic, as far as the gastrointestinal tract was concerned. In the few cases in which digestive symptoms occurred, they presented no specific features. In only 1 instance was there evidence that the administration of hydrochloric acid may have had some beneficial effect.

Pollard and Bloomfield (*loc. cit.*) state that the present report really sets the problem rather than answers it, and it remains to show the underlying lesion responsible for the disorder of secretion and the effect of the presence

of complete anacidity on ultimate general health

A further question of special importance is whether anacidity of this sort is followed in a large percentage of cases by the development of cancer of the stomach, a point that has recently been raised again by A F Hurst (*Lancet* 2 1023 (Nov. 16) 1929) and the writers

With these problems in mind an "anacidity clinic" has been started. The patients are seen periodically; they are interviewed and examined, and x-rays and gastric analyses are made repeatedly. If any of the patients die, it is hoped that pathologic examination will be possible. At any rate, a further report is planned by Pollard and Bloomfield after a sufficient interval, probably 5 or 10 years, has elapsed.

#### IN GALL-BLADDER DISEASE.

—E L Eggleston (*J A M A* 97 1216 (Oct 24) 1931) found 13 per cent of patients with achlorhydria to be suffering from chronic cholecystitis, substantiating his findings by the work of W F Cheney (*Oxford Univ Press* 2 103, 1928), who found achlorhydria present in 25 per cent of cases of chronic cholecystitis and suspects gall-bladder disease in cases of apparent idiopathic chronic gastritis.

**IN ANEMIA.**—As a result of their studies of pernicious anemia, W. B. Castle, W. C. Townsend and C. W. Heath (*Am J M Sc* 180 305 (Sept) 1930) declare that the disease is the result of defective gastric digestion of protein. They believe that the lacking substance is not hydrochloric acid nor pepsin, but an organic thermolabile substance which unites with protein in the stomach to form a hematopoietic substance responsible for the production of the red blood cells. In the absence of

pepsin and hydrochloric acid, the substance may be produced by the stomach for an indeterminate long time, but cases of such achylia are potentially cases of pernicious anemia. This opinion is strengthened by the fact that cases of subtotal gastrectomy sometimes resemble pernicious anemia in their blood findings.

Further studies were conducted by W. B. Castle, C. W. Heath and M. B. Strauss (*Ibid* 182 741 (Dec) 1931) of patients with apparently normal gastric juice, who were from their blood picture typical cases otherwise of pernicious anemia. They found that the existing tests for hydrochloric acid, pepsin and rennin of the gastric juice are not necessarily related to the presence or absence of the substance that acts on protein in the stomach to form the hematopoietic substance. They find there is evidence to indicate that in sprue, other diarrheas, and in some gastrointestinal conditions with sinus formation between various loops of intestine, which cut down the absorbing ability of the gut, there is a lessened absorption of the hematopoietic substance and, therefore, a diminished production of red blood cells, although their experiments with the gastric juice of these same patients (which they combined with beef muscle and then administered to other pernicious anemia cases) shows their gastric juice to contain the necessary substance, which, combined with beef muscle, produces hematopoiesis.

**ANAPHYLAXIS.**—A possible explanation for the horse serum anaphylaxis in man is given by B. Ratner (*J A M A* 94 2046 (June 28) 1930) in which he states that an anaphylactic relationship exists between horse dan-

der and its homologous serum. The common substance present is resident in the globulin fraction of the respective antigens. If guinea-pigs are sensitized to horse dander they may be shocked with horse serum and the reverse is also true, although it is very rare.

This method has been further demonstrated by the inhalation method which is similar to the one to which the human individual is subject. Animals naturally sensitized through the inhalation of horse dander could be killed by anaphylactic shock by the intravenous administration of horse serum or diphtheria antitoxin. Clinical cases are also presented by the author to show that anaphylactic death and accelerated anaphylactic reactions following the primary injection of horse serum or horse serum antitoxin occur in those individuals spontaneously hypersensitive to horse dander. Although human beings may be artificially sensitized by large injections of horse serum, they are less susceptible to anaphylaxis than the spontaneously sensitized person with horse asthma. The author stresses the point that if it is imperative to administer horse serum for therapeutic purposes, the greatest precautions should be observed to give the serum exceedingly slowly and by the route of least absorption coupled with the utilization of such drugs as epinephrin and atropine.

W. M. Sheppe (J. Lab. and Clin. Med. 16:372 (Jan.) 1931) reports a case of sudden death with complete postmortem observations, following the injection of foreign protein. It is believed to be a bronchioplastic type of true fatal anaphylaxis. Fifteen other cases coming to autopsy are analyzed and 13 of these are considered as true anaphylaxis in man.

In each instance death occurred

associated with a bronchial spasm or splanchnic dilatation. The theory is advanced that an entirely new mechanism (possibly thymolymphatic) is responsible for post-injection death not exhibiting bronchospasm or splanchnic dilatation at autopsy. The author urges that all cases of this type be subjected to postmortem examination for (a) elimination of other and unsuspected causes of death, (b) recording of careful observations relative to the condition of the pulmonary, thymolymphatic and splanchnic systems, and (c) accurate classification of the type of reaction based on anatomic observations and considerations.

A case of fatal anaphylactic shock after a single injection of diphtheria antitoxin is reported by I. G. M. Bullowa and M. Jacobi (Arch. Int. Med. 46:306 (Aug.) 1930). An acute pulmonary emphysema, dilatation of the right heart, general venous stasis and visceral congestion existed, the left heart being empty and contracted. According to the authors, the pathogenesis of this fatal shock consisted chiefly of overfilling of the lungs which remained distended; a drop in the peripheral blood-pressure with a concomitant rise in the pulmonary arterial pressure; a progressive weakening of the cardiac contractions, and a slowing and final stopping of the heart, with the right auricle and ventricle in diastole and very much dilated.

A case of spontaneous hypersensitivity to animal serum is reported by A. V. Neale (Brit. J. Child. Dis. 27:113 (Apr.-June) 1930). The clinical history was indicative of an allergic condition as the child suffered from asthma since early life. Thirty minutes after the injection of 2 c.c. (32 minims) of animal serum, death occurred from

respiratory and circulatory failure. A conspicuous feature, postmortem, was a complete absence of coagulation of the blood

**ANEMIA, PERNICIOUS.**—In an excellent article, summarizing present knowledge on primary anemia, J. Vaughan (Univ College Hosp Magazine (Apr-May) 1931) has quoted Cornell ("Pernicious Anemia," Duke University Press, Durham, 1927) as defining pernicious anemia as a disease of unknown etiology, showing a characteristic triad of changes in the digestive, blood and nervous systems. She further quotes him as saying that exactly similar changes are found in close association in other conditions (1) in sprue; (2) in that ill-defined condition, the pernicious anemia of pregnancy, (3) in severe lesions of the gastric tract, as carcinoma of the stomach, multiple anastomoses, gastrectomy and obstruction due to tuberculous glands

In this paper the above mentioned diseases are, therefore, studied together in the attempt to analyze the etiology of what the author calls "Addisonian pernicious anemia."

**PATHOLOGY.**—The pathological changes are discussed under 4 headings. (1) The hemopoietic system, *i e*, those organs concerned in blood production and blood destruction, (2) the digestive system; (3) metabolism; (4) the central nervous system

**A Alterations in the Hemopoietic Organs.**—1 *Bone-marrow*—The bone-marrow is found to be hyperplastic throughout the body, the marrow being bright red in the cavities or the long bones. This is not found to so marked a degree in the anemias with active regeneration, such as in acholuric jaundice. Vaughan quotes F. W. Peabody

(Am J Path 3 179 (May) 1927) as saying that during relapse, the essential histological lesion is a rapid and extensive proliferation of primitive cells (megaloblasts) with a relatively diminished tendency towards the differentiation of mature cells of the erythrocyte series. The bone-marrow shows a cellular hyperplasia, but it is functionally inefficient

It is a mooted question as to the origin of the megaloblast. Sabin and her followers consider it as a normal cell present in abnormal numbers in pernicious anemia. A Piney ("Recent Advances in Hematology," Churchill, London, 1927) considers the megaloblast is an abnormal cell in the adult blood. It may, however, be found in the bloodstream in any severe anemia with active regeneration

If it is an abnormal cell, it is difficult to understand how it gives way so rapidly to normal cell production under liver therapy

For the purposes of the article, Vaughan uses the term to signify a primitive red cell which appears to mature, giving rise to erythroblasts capable of becoming normal adult red cells. She cites Peabody's reports of cases undergoing liver treatment, *viz*, "Remissions are characterized by the presence of few megaloblasts and a great relative increase of normoblasts and mature red blood-cells in the bone marrow."

This megaloblastic hyperplasia has been described by F. P. Mackie (Indian J Med Research 16 827 (Jan) 1929) as occurring in sprue, and it has been reported unsatisfactorily that it occurs in the pernicious anemia of pregnancy.

2 *Blood Picture*—This is characterized in anemia by a high color index, usually over 1, a leukopenia with relative lymphocytosis and a great variation

in size of the red blood-cell, with a predominance of large cells or macrocytes

(a) *Price-Jones Curve*—The change in the blood picture is shown best by plotting the number of cells against the diameter. In the normal this curve is symmetrical, the average mean for 100 healthy adults by the dry film method being 7202  $\mu$ , the healthy range being from 6686  $\mu$  to 7718  $\mu$ . In pernicious anemia it is very uneven and shifted to the right, showing an average diameter of 824  $\mu$ . In secondary anemia due to hemorrhage it is shifted to the left and shows less irregularity, C. Price-Jones (Path and Bact 32 479 (July) 1929), (*Idem Ibid* 25 487 (Oct) 1922). She further quotes Price-Jones as reporting 3 possibilities following liver therapy (1) The curve may return completely to normal, (2) variability may recover but not size; (3) size may return to normal but variability be unaffected. It is possible that the 2 latter cases may be an indicator of the adequacy of the dosage, and be brought within the range of normalcy by modifying the therapeutic procedure.

(b) *Reticulocyte Response*—As G. R. Minot and W. P. Murphy (J. A. M. A. 87. 470 (Aug 14) 1926) first described, in 1926, the feeding to patients with idiopathic pernicious anemia of an adequate amount of liver is followed by changes in the circulating red blood-cells. On the sixth to the tenth day the number of reticulocytes in the circulating blood starts to rise rapidly, reaching a high figure and then falling again to a normal level of 1.1 to 0.1 per cent. This is indicative of bone-marrow activity and is not peculiar to pernicious anemia nor to liver therapy; it merely indicates the therapeutic value of the substance used in the treatment of the anemia.

The duration and height of the reticulocyte count is, according to G. R. Minot, E. J. Cohn, W. P. Murphy, and H. A. Lawson (Am J M Sc 175 500 (May) 1928), dependent upon 2 factors which can be determined accurately (1) The initial level of the red blood-cell count, (2) the amount of active principle given. A third possible factor is the exact state of the bone marrow. It is possible to predict within 2 per cent. the level to which the reticulocytes should rise if a maximum dose is given—the response is prolonged and shows an uneven curve when submaximum doses are given.

The nature of this response has been followed closely by M. C. Riddle and C. C. Sturgis (Am. J. M. Sc. 180. 1 (July) 1930). The time of the first appearance of reticulocytes appears to be entirely dependent upon the concentration of the active principle.

It is difficult to feed more than  $\frac{1}{2}$  pound (240 Gm.) of whole liver a day by mouth. The rise under such circumstances occurs about the sixth day. If extract 343 N. N. R. is given in a single massive dose of 30 tubes, or the equivalent of 3000 Gm. (6 $\frac{1}{2}$  pounds) of liver, the response begins within 48 hours, the maximum number of reticulocytes occurring between 104 and 140 hours. Megaloblasts appeared, in 1 case, within 8 to 16 hours, being gradually replaced by normoblasts in 32 hours and by the forty-eighth hour only an occasional nucleated red cell was present and the reticulocytes started to rise.

(c) *White Blood-cells*.—W. E. Cooke and E. Ponder ("The Polynuclear Count," Chas. Griffin and Co., London, 1927) have shown, according to Vaughan, the distinctive character of the polymorph leukocytes in pernicious anemia. There is a shift of the Arneith



count to the right, with a marked lobulation of the nucleus, which returns to normal with treatment. Riddle and Sturgis (*loc cit*) claim that immature white cells may also appear in the bloodstream within the early hours of treatment. The leukopenia tends to be lost as the patient's condition improves. The eosinophilia which accompanies liver therapy is apparently insignificant, as it appears in normal people when fed raw liver.

3 *Liver*—If megaloblasts are derived from the cells belonging to the reticulo-endothelial system, it is reasonable to expect changes in this system other than in the bone-marrow. S. R. Mettier (Arch Path 8 213 (Aug) 1929) found such changes in the Kupffer cells of 20 patients who died during a relapse, in comparison with 5 others who died from other causes while in a remission. Pigment was found both in the Kupffer cells and in the liver cells. No evidence in support of Piney's observations that megaloblastic tissue, a remnant of fetal blood formation, is found, was forthcoming.

4 *Spleen*.—The spleen is often enlarged, denoting a deranged function, as is found in the rest of the hematopoietic system. The variability of the histological findings suggests that the changes in the spleen are secondary and not intimately connected with the etiology of the disease.

**Chemical Changes.**—Certain changes in the blood chemistry appear to be associated with the hemopoietic system activity, *ie*, (1) alterations in bile-pigment metabolism; (2) alterations in iron metabolism, (3) alterations in uric acid; (4) alterations in cholesterol.

1. *Bile-pigment*—The van den Bergh reaction is usually positive indirect. N. H. Fairley (Tr Roy. Soc Trop.

Med and Hyg 24 131 (Aug) 1930) in comparing sprue and Addisonian pernicious anemia, quotes a reading of 12 units as an average in the latter, which is a somewhat lower figure than is found in the former. A remission following liver therapy is accompanied by a return of the serum bilirubin to normal.

2 *Iron*—At autopsy the organs, especially the liver and kidneys, show marked siderosis. This is not surprising because it is known that iron is closely associated in the process of blood production. H. H. Riecker (Arch Int Med 46 458 (Sept) 1930) claims to have shown that the level of serum-iron is higher than normal in pernicious anemia, becoming normal during a remission. The variations detected were small, and too much emphasis cannot be laid upon them.

3 *Uric Acid*—Nuclear metabolism is closely associated with uric acid metabolism. It is, therefore, not surprising to find alterations in the uric acid metabolism during a remission when there is a rapid change from a nucleated red cell production to a normal adult red cell production.

M. C. Riddle (J Clin Investigation 8 69 (Dec) 1929) showed that the blood uric acid which was on the low normal side before treatment rose to as high as 10 mg per 100 c c at the height of the reticulocyte response, while the output of uric acid which was normal before treatment increased within 48 hours, reaching high levels in association with the reticulocyte crisis. Recent experimental support has been given to the hypothesis that such changes are dependent upon nuclear destruction associated with active blood production. J. Krafka, Jr. (J Biol Chem 86 223 (Mar.) 1930), the work being done

on Dalmatian dogs. It is independent of the effect of feeding liver extract in which the effective principle has been destroyed, and it was without effect on either the reticulocytes or the uric acid level, while a patient undergoing spontaneous remission showed similar changes. How far these effects are peculiar to pernicious anemia cannot be at this time stated and observation data is not yet available on the variation in uric acid in other anemias. Numerous studies are now in progress.

4 *Cholesterol*—Little is known of the significance of the change in the blood cholesterol. G. L. Muller (Am. J. M. Sc. 179:316 (Mar.) 1930) reports that during the relapse the cholesterol and lecithin phosphorus is low, while there is little or no variation in the fatty acids. With the onset of a remission, the cholesterol suddenly rises simultaneously with the rise in the reticulocyte count and, like the reticulocyte count at the height of the rise, is dependent upon the initial red blood cell count. This increase in cholesterol occurs before there is a definite increase in the concentration of hemoglobin or red blood-cells. It is associated with the remission, irrespective of the form of therapy employed. Healthy individuals show no such changes in cholesterol value when fed whole liver; therefore, the low cholesterol in pernicious anemia and rise occurring in remission would appear closely associated with the disease itself. Exactly similar changes are reported by Fairley in cases of sprue on liver treatment.

Work by W. MacAdams and C. Shiskin (Quart. J. Med. 16:193 (Apr.) 1923) indicates that the blood cholesterol is lowered in acholuric jaundice with anemia, and that it rises to normal after splenectomy. This would suggest

that the low cholesterol is associated with anemia *per se*.

B *Digestive System* 1 *Gastric Function*—The usual insufficiency of gastric function is demonstrated in the lack of (1) free hydrochloric acid; (2) pepsin and rennin, (3) a factor responsible for protein digestion.

(a) *Hydrochloric Acid*—The statistical studies of Cornell puts the absence of free hydrochloric acid at 99 per cent. This is probably too high. I. S. P. Davidson and G. I. Gulland ("Pernicious Anemia," Kempton, London, 1930). C. C. Ungle (Newcastle M. J. 10:14 (Oct.) 1929) report cases in which there was adequate acid secretion and Goodhart (unpublished record) has allowed the author of this article (Janet Vaughan) to mention a case which repeatedly showed free acid with typical pathological changes at autopsy. Treatment appears to be without effect on this deficiency in the case of idiopathic anemia.

Achlorhydria is present in those cases of intestinal lesion associated with the pernicious anemia syndrome, also in the severe anemia of pregnancy, but the presence of acid in sprue shows that a megalocytic anemia is not invariably associated with achlorhydria.

(b) *Pepsin and Rennin*—The significance of the reduction of pepsin and rennin is little understood at this time. It is of interest, however, that J. F. Wilkinson (Brit. M. J. 1:236 (Feb. 8) 1930) considers the peptic activity of any desiccated stomach preparation to be indicative of its therapeutic value.

(c) *Protein Digestion*—Recent reports by W. B. Castle (Am. J. M. Sc. 178:748 (Dec.) 1929) and W. B. Castle, W. C. Townsend, and C. W. Heath (*Ibid.* 180:305 (Sept.) 1930; Lancet 1:1062 (May 17) 1930) em-



phasize the extreme importance of the deficiency of some factor concerned in protein digestion. It was found that beefsteak digested in the healthy normal stomach and then fed to pernicious anemia patients was effective in inducing a remission. Beefsteak or healthy gastric juice alone fed separately were without effect. J. F. Wilkinson (*loc cit*) repeated Castle's experiments with a good effect, using gastric juice alone. W. J. Middleton repeated Wilkinson's observations, gave the juice with food, and obtained a slight reticulocyte response. Similarly, beefsteak digested with healthy gastric juice *in vitro*, under suitable conditions, was effective. The result of interaction of beefsteak and gastric juice is independent of rennin, pepsin, or the hydrochloric acid content of the latter. In a megalocytic anemia with an apparently normal gastric secretion which contained hydrochloric acid, pepsin and rennin, the patient failed to respond to a large daily intake of beefsteak, showing that this gastric juice was deficient in the production of the effective principle *in vivo*. When drained off and added to beef muscle under suitable conditions and fed to a patient with idiopathic pernicious anemia, no effect was apparent, yet both the donor and the recipient reacted well to a known positive preparation, proving that this juice was equally incapable *in vitro*. An exactly similar experiment was carried out, using the gastric juice of a patient with megalocytic anemia, complicated by multiple intestinal anastomoses. The gastric juice was apparently normal but was inactive when added to beefsteak and fed to a patient with pernicious anemia.

Due to rapidity of postmortem changes in the stomach, satisfactory studies have not been carried out but A.

F. Hurst and J. R. Bell (Bram. 45·266 (Oct.) 1922) believe that primary achylia is not dependent upon anatomical lesions, but is itself responsible for the gastritis so often found.

**2 Tongue**—The sore tongue often seen in conjunction with Addisonian pernicious anemia is not pathognomonic of this disease, as it is seen in many of the deficiency diseases—in severe microcytic anemia associated with iron deficiency; in anemia due to undernutrition, in the Plummer-Vincent syndrome and in pellagra.

Its cause is still unknown.

Several causes are suggested. Atrophic lesion due to nervous dysfunction, but it occurs in cases where there appears to be no nervous involvement, the presence of achlorhydria, but cases of sprue in which there is sufficient free hydrochloric acid associated with a megalocytic anemia seems to rule this out as a cause, cases of severe microcytic anemia in women with achlorhydria and a typical tongue have been shown not to be deficient in the factor essential for protein digestion and cases have been cited in which this essential principle was deficient and the tongue was normal, so the absence of the principle essential to protein digestion cannot be considered the etiological factor. Sepsis has been suggested, but not all cases of microcytic or macrocytic anemia have pyorrhea, although the incidence is high.

**C Metabolism**.—The patient who is about to go into remission feels and looks better before there is any alteration in the reticulocyte count, therefore, it is obvious that there is some very definite change in the body mechanism. Reports show that there is a striking gain in weight irrespective of whether the remission was spontaneous or brought about by liver therapy.

The cause of this gain in weight might be due to any or all of 3 factors, *i.e.*, (1) alteration in basal metabolic rate as occurs in myxedema; (2) retention of fluid, (3) increased caloric intake

1 *Basal Metabolic Rate*—The change in the basal metabolic rate is not sufficient to account for the weight gain or the psychological improvement in the patient

2 *Weight Gain*—The weight gain coincident with a remission shows 2 peaks. The first comes with the reticulocyte rise and the second with the improvement in the red cell count. The first peak occurs in the majority of patients regardless of their caloric intake and is followed by a loss of weight. It is also accompanied by a retention of fluid and even the appearance of edema in some cases. The loss of weight, following the first gain, is accompanied by an increase in the output of fluid and diminution of the edema. The second peak of the gain in weight then occurs, proportional to the caloric intake, which appears to be the most important factor in the final body weight increase

*D Central Nervous System.*—Due to the frequent lack of troublesome nervous symptoms only 5 per cent. of the cases of megalocytic anemia are reported by Davidson and Gulland as showing definite evidence of cord damage, whereas some authorities claim that serious involvement is demonstrable in 80 per cent. of the cases, the nervous complaints in the latter figure including paresthesias and tinglings. These figures are probably both wrong, 50 per cent being nearer correct, with the incidence of nervous involvement higher in the older cases

Due to the presence of edema, the cord is considerably enlarged; micro-

scopically there are areas of degeneration scattered throughout the white matter irrespective of the tracts; later there may occur changes in the grey matter secondary to the damage of the tracts in the white matter. J. Collier (*Subacute Combined Degeneration* "Textbook Practice of Medicine" F. W. Price, 2d Edit., H. Frowde, London, 1926) emphasizes the point that, regardless of how long-standing the case may be, there is practically no neurological proliferation, the end result being fatty degeneration of the medullary sheaths followed by vacuolation

The effect of liver on these lesions was considered negligible, according to earlier clinical reports, but recently the reports are more satisfactory. Many cases of recovery of even severe organic lesions are being reported (G. O. Brown, O. Ames, S. Warren, and F. W. Peabody. *J. Clin. Investigation* 1: 295 (Feb.) 1925; C. C. Ungley and M. M. Suzman: *Brain* 52: 271 (Sept.) 1929).

In Ungley's report he is quoted as saying: "From clinical evidence, all signs and symptoms of cord involvement may disappear; it would appear that degenerative changes in the white matter in this disease are not necessarily of a permanent character." From an analysis it seems that the cases of shortest duration show best nervous recovery, "suggesting that," according to Vaughan, "complete degeneration is a late stage."

**LIVER TREATMENT.** Analysis of the literature indicates that the anemias showing the most spectacular response to liver are those belonging to the pernicious anemia syndrome, *i.e.*, Addisonian pernicious anemia, sprue, the pernicious anemia of pregnancy and the megalocytic anemias associated with intestinal lesions. J. M. Vaughan (*Quart. J. Med.* 23: 213 (Jan.) 1930)

also found that this group alone responds satisfactorily to liver extracts. Most observers agree that secondary anemia following hemorrhage responds very well to whole liver given alone or in combination with iron, in fact, C S. Keefer and C S Yang (*Nat M J China* 15 701 1929, *J A M A* 93 575 (Aug 24) 1929), who have had considerable experience with the anemias of malnutrition, coincident in many cases with parasitical infections, invariably found whole liver in conjunction with iron more beneficial than any extract.

G H Whipple, F S Robschelt-Robbins, and G B Walden (*Am J M Sc* 179 628 (May) 1930) recently reported satisfactory results in treating dogs rendered anemic by hemorrhage, with an extract prepared from the waste product of the manufacture of the pernicious anemia fraction, the belief being that there is a second factor present in liver. No reports are available at present of the treatment of clinical secondary anemias with a similar preparation.

It is now generally accepted that although liver is valuable in treating many, if not all, forms of anemia, it contains some specific factor which is of particular benefit in the treatment of anemias presenting the pernicious anemia syndrome.

**ETIOLOGY.**—In the discussion of the pathological changes in those conditions presenting the pernicious anemia syndrome it was noted that these cases show a deficiency in the gastric digestion of protein as well as a bone-marrow hyperplasia. The relegation of achlorhydria as a factor of secondary importance in the production of the pernicious anemia syndrome in favor of some deficiency in protein digestion is not accepted by R Glanvill and A. F. Hurst (*Guy's Hosp Rep.* 80:411

(Oct) 1930). These observers produce evidence that a patient recovered a normal blood-picture after gastro-jejunostomy on the addition of hydrochloric acid alone, and they also describe a case in which achlorhydria resulted from the same procedure, and the patient developed a typical chlorotic anemia, it appears, therefore, that neutralization cannot be the only factor.

As reported by Cornell, Addisonian anemia which appears typical in every way may develop in the presence of hydrochloric acid. Cases of sprue showing a typical megalocytic anemia and responding favorably to liver therapy may have free hydrochloric acid in the gastric juice. Castle has demonstrated the deficiency in such cases of the factor concerned with protein digestion; also in a case of multiple anastomoses, though free hydrochloric acid was present in both cases.

If the absence of hydrochloric acid is a factor in the production of pernicious anemia, it may be through its effect on the absorption of iron.

**MODE OF ACTION OF LIVER EXTRACT.**—The cases of anemia responding to liver extract most favorably are those characterized by a megaloblastic bone-marrow, therefore, the effective principle must exert its influence upon the development of the megaloblast, either directly or indirectly.

J M Vaughan, G L Muller and L. Zetzel (*Brit J Exper Path* 11.456 (Dec) 1930), experimenting with the grain-fed pigeon, raised the level of the reticulocyte count from a normal level of 8 to 10 per cent to about 20 per cent on the administration of liver preparations intravenously, the reticulocytes becoming more immature in type. The same result was obtained when extract 343 N. N. R. was given by mouth,

unless sepsis was present. This is practically the result obtained in clinical practice. No such results were obtained with inactivated extracts or certain control materials. G. L. Muller (Am J Physiol 88:130 (Feb.) 1929) also reported definite changes in the bone-marrow of pigeons exclusively fed on liver diet.

The experiments seem to show that the effective principle enables the megakaryoblast to mature. In the absence of this effective principle the megakaryoblast proliferates, due to its inability to develop in a normal manner.

**Red Cell Production.**—The production of the normal red cell requires iron and pigment, therefore, the excess of these 2 substances disappears from the serum as soon as the megakaryoblasts begin to mature.

Recent evidence tends to support Erhlich's hypothesis that the anemia is dependent upon deficient production; since few red cells are being produced, the iron and other pigments resulting from destruction of red cells accumulate in the tissues and blood-stream, producing an excess; the normal or even negative balance being established when blood production is stimulated.

Recent observations seem to indicate that the effective principle of liver acts primarily on the stroma and development of the red cells, while the pigment utilization is only secondarily affected.

**NATURE OF DEFICIENCY.**—Little can be said of the deficiency of gastric secretion, but in the case of Addisonian pernicious anemia it appears to be permanent. In the anemias occurring in sprue and pregnancy this gastric function is completely restored and remains so even after cessation of therapy. The cause of this gastric deficiency is unknown and in the case of Addisonian

pernicious anemia it has been suggested that there is an hereditary tendency, while in sprue and multiple anastomoses the gastric dysfunction appears to be an acquired condition.

It has been calculated that the incidence of pernicious anemia is about 1 in 20,000 and the appearance of the disease in more than one member of a family is striking.

Observation on the causative factor of the achylia has resulted in presentation of data in favor of and against the presence of streptococci in the intestinal flora, but no conclusive evidence has yet been offered. In fact the development of the gastric insufficiency is inexplicable except on the ground of an hereditary tendency.

**EFFECTIVE PRINCIPLE.** R. West, M. Howe and H. D. Dakin (Proc Soc Exper Biol and Med 28:512, 1931) have recently isolated the effective principle from liver. It is a combination of  $\beta$ -hydroxyglutamic acid and  $\alpha$ -hydroxy proline; the extract linkage has not yet been determined. The method of formation and the final distribution is also not yet known.

It appears that the action of hog's stomach in the production of a remission is dependent upon a process of protein digestion occurring in the preparation itself, because if the muscle wall is fed alone there is no response; if the mucous membrane is fed alone there is scarcely any response; when fed together it is suggested that the enzyme present in the mucous membrane digests the protein of the muscle layers, with a consequent elaboration of the active principle or its precursor.

Wilkinson, as well as C. C. Sturgis and R. Isaacs (Am. J. M. Sc. 180:597 (Nov.) 1930) have shown that hog's stomach preparations are as effective as

liver; it is, therefore, suggested that the digestion of protein by gastric juice elaborates the essential principle while the liver and kidneys merely act as storage depots

The isolated principle is extremely potent and West (H D Dakin, R West and M Howe *loc cit*), in his preliminary report, gives no idea of the dosage employed. Other workers on the location of the effective principle claim that the action is increased 3000 times as compared with liver when the most potent preparations are given intravenously, suggesting that the active principle is present in this organ in very minute quantities, which seems to be analogous with the action of other glandular extracts and the vitamins

Due to the discrepancies between the blood-cell count and nervous symptoms, Ungley suggests "that the specific substance in the liver diet which benefits the neurological symptoms is a different one from the hemopoietic factor"

E F Gildea, E E Kattwinkel and W B Castle (New England J. Med., 202 523 (Mar 13) 1930) have brought forward experimental evidence in favor of the antineuritic factor, **vitamine B**, as being the deficient factor. Castle, working with Minot, found that large doses of the vitamine may relieve cord symptoms in human cases

Further work with the active principle isolated by West will perhaps solve the problem as to the etiological relationship of the cord lesions and the marrow abnormalities

**Treatment.**—*Mode of Administration*—The effective principle may be administered by (1) mouth, (2) rectum; (3) intramuscularly, (4) intravenously

Extracts are as effective as whole liver or stomach in the *megalocytic an-*

*emias*, but they vary in potency. It is suggested that if a satisfactory response is not obtained with a certain extract, either the extract should be changed or the dose increased. In the use of stomach preparations Wilkinson emphasizes the fact that there is considerable variation in the potency and suggests that the peptic activity indicates the effectiveness of the preparation. He also believes that certain cases respond better to the stomach preparation than to the liver and *vice versa*. This, however, awaits confirmation by other observers

In the use of liver, large amounts must be given daily, due to the low active principle content. If, however, the extract of either liver or stomach is used, an initial massive dose may be given to start a remission, followed by the daily dosage

The advantage of a large initial dose is important in treating the extremely ill patient as a response is obtained in 48 hours, while with the daily dosage method 6 or more days are required to produce the same effect. If the patient is too ill to cooperate, the substance should be given through a stomach tube and if vomiting is present dilute hydrochloric acid may be added. If vomiting still persists, equally large quantities may be given in saline or glucose solutions

Only the liver extracts have been reported as having been given intramuscularly and, despite the absence of full detail, are apparently satisfactory

Preparations for intravenous administration are as yet not generally available but the value of this form of therapy to moribund patients is obvious. There is evidence to support the fact that certain refractive cases are controlled by this method when oral administration has proved unsatisfactory.

**Factors Influencing Action of Effective Principle.**—Factors which appear to influence the response to liver, both in the acute stage and later, are: (1) sepsis, (2) the presence of central nervous lesions; (3) the presence of arteriosclerosis, (4) iron deficiency, and (5) an associated thyroid deficiency.

1 *Sepsis*—As in the case of insulin in diabetes, the influence of the treatment is less satisfactory in the presence of sepsis. If a satisfactory blood level is not maintained, therefore, in cases taking an adequate amount of liver, a thorough search for a focus of infection should be made. The reason for the deleterious effect of sepsis is not satisfactorily explained.

2 *Central Nervous Lesions*—It is noted that cases with central nervous system lesions require a larger maintenance dose than cases uncomplicated by such lesions. The reason for this is also unknown.

3 *Arteriosclerosis*—Not only in pernicious anemia, but in the development of other deficiency diseases, especially scurvy and pellagra, is the thickening of the vessels noted. The part played by this condition, especially in the elderly subject is suggested as a failure of satisfactory absorption.

4 *Iron Deficiency*—The paradox of iron deficiency, with siderosis of liver and kidneys, is explained by the fact that although the iron is present, it is not being utilized; with a return of normal hemopoietic activity there is frequently an actual lack of sufficient iron. Therefore, in a patient whose red-cell count rises without a relative rise in hemoglobin, a thought should be given to the possibility of a lack of iron. This has been given in the form of **Blaud's mass** or **iron ammonium citrate** which has proven satisfactory.

5 *Myxedema*—Cases of myxedema may complicate the picture in 2 ways. It may lead to the wrong diagnosis. Cases have been reported by G. M. Mackenzie, (*J. A. M. A.* 86: 462 (Feb. 13) 1926) with a blood-picture similar to pernicious anemia which were relieved by thyroid treatment. It is also suggested that these 2 conditions may exist together.

The basal metabolic rate is usually raised in Addisonian pernicious anemia, unless complicated by myxedema, when it is lowered. A routine basal metabolic determination is suggested by some observers and if found to be subnormal, **thyroid therapy** as well as **liver** should be tried.

Occasionally with the addition of thyroid to the treatment there is a marked improvement in the hematological and clinical picture.

**Additional Treatment.** **Hydrochloric acid**, although not used as extensively as before the introduction of liver therapy, still has a place in the armamentarium of the physician treating pernicious anemia. There is no doubt that it certainly relieves the digestive symptoms of a patient taking liver. It is shown by S. R. Mettier, and G. R. Minot, (*Am. J. M. Sc.* 181: 251 (Jan.) 1931) that small doses of iron are more readily absorbed in an acid medium than in an alkaline medium; also, in the case of severe vomiting it may serve to control this distressing symptom.

The general diet should be adequately balanced and contain food rich in **vitamine B**, which was shown earlier in the article to be useful in the treatment of cases presenting a nervous lesion.

**CONCLUSION.**—The conclusions drawn by Vaughan (*Univ. College Hosp. Magazine* (Apr.-May) 1931) in this extremely well presented paper



are as follows Anemias associated with the pernicious anemia syndrome must be regarded as deficiency diseases, dependent upon a common factor, namely, the lack of some product of protein digestion due to faulty gastric function Treatment attempts to remedy this deficiency by supplying the essential principle already elaborated and, to be effective, adequate dosage is essential

**PATHOLOGY.**—In a study of *oxygen consumption and nitrogen metabolism* in pernicious anemia, C W Baldridge and A P Barer (J Clin Investigation 10 529 (Aug) 1931) observed that early in induced remissions the influences which cause a lowering of the oxygen requirement are usually potent enough to counteract the effect of 2 factors which might in themselves aid to increase the oxygen requirement during this period These factors are (1) the increased oxygen requirement of circulating reticulocytes, and (2) the increased oxygen required to maintain the high level of endogenous uric acid metabolism which exists During an active relapse blood cells are being destroyed more rapidly than they are formed, and there is a negative nitrogen balance with an increased oxygen consumption During induced remissions blood cells are being formed much more rapidly than they are being destroyed and there is nitrogen retention with a decreasing oxygen consumption The following is suggested as a working hypothesis There is a direct causal relationship between the increase in nitrogen catabolism and increased oxygen consumption, and a similar relationship of cause and effect between nitrogen storage and decrease in oxygen requirement

In a study of the *nervous lesions* in 115 cases of pernicious anemia by K. C.

Smithburn and L G Zervas (Arch Neurol. and Psychiat 25 1100 (May) 1931), these authors observed the following neural symptoms and signs 96.6 per cent of the patients showed some evidence of neural involvement, 30.4 per cent had marked neural manifestations, 6 per cent had definite psychoses

Improvement may occur in the neural and psychic changes in patients with pernicious anemia under treatment with adequate amounts of liver extract, but may be due in part or wholly to improvement in the general condition

In some cases arrest of the neural and psychic symptoms, without improvement or retrograde change, may occur Neural and psychic changes may develop for the first time or may steadily progress while the patient is being treated with daily amounts of liver extract adequate to maintain a normal erythrocyte level Liver extract apparently does not contain any specific antineurotoxic substance

Regardless of the preceding conclusion, it is advisable to administer daily amounts of potent liver extract adequate to maintain the general health and normal level of red blood cells and to take precautionary measures to avoid intercurrent infections During intercurrent infections or in the presence of increasingly severe neural manifestations, it may be advisable to administer maximal amounts of a potent fraction of liver

**DIAGNOSIS.**—Seven out of a series of 150 cases were selected by J F. Wilkinson and W Brockbank, (Acta. med. Scandinav 74 211 (Dec. 16) 1930), in order to illustrate the *difficulties* often encountered in making an early diagnosis It is suggested that, besides a complete blood examination, a fractional test meal should be a routine procedure in all cases of weakness and

anemia, persistent diarrhea, and soreness of the tongue, in all cases of pares-  
thesis, and all undiagnosed cases of gas-  
trointestinal disease, particularly those  
of doubtful carcinoma of the stomach

T A C Rennie (J Lab Clin Med  
16.557 (Mar) 1931) considers that  
the definitely frequent occurrence of  
disturbed *dextrose tolerance* in perni-  
cious anemia points to a similarity be-  
tween certain features of this disease  
process and diabetes mellitus

Improvement in the blood pictures  
of all the patients studied by treatment  
with from 30 to 40 Gm (1 to 1½  
ounces) of desiccated defatted hog  
stomach was accompanied by increased  
dextrose tolerance

S Nittis (Ann Int Med 4 931  
(Feb) 1931) believes that there is no  
gross correlation between the increase  
in numbers of the *platelets* and that of  
the erythrocytes, the reticulocyte per-  
centage or the number of leukocytes.  
Giant forms of blood platelets appear  
and disappear at intervals in all cases,  
but this phenomenon does not form a  
markedly regular rhythm

**Neutral Red Test.**—Three cases  
have been reported of patients with per-  
nicious anemia in whom injected neu-  
tral red was recovered in the gastric  
extractions. Previous investigators, ac-  
cording to S J Cohen, M J Matzner  
and I Gray (Arch Int Med 46 979  
(Dec) 1930), have emphasized the diag-  
nostic value of the neutral red test in  
pernicious anemia, but they have never  
before been able to recover neutral red  
in the gastric specimens in true perni-  
cious anemia. The value of the test for  
neutral red is always questionable, be-  
cause the presence of the dye in the  
stomach may be accounted for by re-  
gurgitation of duodenal content

A simple and rapid method for the

detection of neutral red in the gastric  
content given by these authors is as  
follows

A Rehfuß tube is introduced into the  
“fasting stomach” and the stomach is washed  
with water until the contents return water  
clear. Two cc (½ dram) of a 2 per cent  
solution of neutral red (40 mg—¾ grain)  
is injected intramuscularly into the gluteal  
region. The stomach specimen is then aspir-  
ated and placed in a separate test-tube every  
15 minutes for 2 hours. If there is little or  
no gastric secretion, 15 or 20 cc (½ to ¾  
ounce) of water may be introduced and aspir-  
ated as the next specimen 15 minutes later

To 15 or 20 cc (½ to ¾ ounce) of the  
stomach contents is added approximately 2 Gm  
(30 grains) of tribasic lead acetate and the  
tube shaken. If the contents seem to contain  
a larger quantity of bile, about 1 Gm (15  
grains) of purified animal charcoal is also  
added. Filter and obtain enough filtrate to  
fill a small test-tube. When smaller quanti-  
ties of the contents of the stomach are used,  
proportionate amounts of the lead acetate and  
charcoal are employed. A few drops of glaci-  
al acetic acid are added to the filtrate while  
it is viewed against a pure white background,  
using a control tube of plain water as con-  
trast. When neutral red is present the solu-  
tion will begin to assume a pinkish color with-  
in a few seconds. The depth of the color is  
proportional to the concentration of the dye.  
No attempt has been made to determine the  
dye quantitatively

The conclusion reached in this report  
is that the presence of neutral red in  
the gastric extractions does not in itself  
exclude the diagnosis of pernicious  
anemia

**X-ray in Diagnosis.**—F B. Mandel-  
ville (Radiology 15 72 (July) 1930,  
states that x-ray examination in *ery-  
throblastic anemia* demonstrates peculiar  
changes in the *bones* of definite value  
in confirming the clinical diagnosis.  
The x-ray observations in bones in 4  
additional cases of erythroblastic anemia  
are presented. Necropsies of 6 cases  
have been made in various medical cen-



ters and reports tend to confirm the x-ray observations

The x-ray studies of *enlarged hearts* due to anemia and to organic valvular disease are often hard to differentiate. The large heart due to anemia may decrease in size with improvement in the symptoms. The murmurs heard in severe anemias often disappear with decrease in severity of the disease. The finding of an enlarged heart and other signs in a patient with a severe anemia does not itself indicate organic heart disease, according to D Ball (Am Heart J 6 517 (Apr) 1931)

**TREATMENT.**—Patients with pernicious anemia were subjected to serial forms of treatment by K Gutzeit and J Herrman (Munchen med Wchnschr. 78 266 (Feb 13) 1931), the following results being obtained (1) In patients receiving daily 250 Gm ( $8\frac{1}{3}$  ounces) of meat that had been exposed for 1 hour to the influence of gastric juice, the symptoms of anemia disappeared (2) The same results were obtained when patients were given meat that had been treated with a pepsin preparation. However, when the same pepsin preparation was given as a medicament in addition to ordinary diet, it had no effect. (3) Since the stomach preparation that proved effective in pernicious anemia does not contain rennin, this substance cannot be the antianemic factor (4) Powder prepared from the mucous membrane of the fundus was effective in counteracting the anemia, a preparation from the pyloric mucous membrane was effective in only 1 out of 3 cases (5) A powder prepared from the wall of the small intestines of the hog proved ineffective.

In patients who fail to respond to liver therapy in the presence of a temperature, good results were obtained by

C S D Don (Brit M J 2 280 (Aug 23) 1930) by using **blood transfusion**.

Antianemic preparations were made from the various portions of the **gastric and duodenal mucous membranes of hogs** and their therapeutic value tested by treating cases of pernicious anemia. The results indicated that the powder prepared from the mucous membranes of the antrum is more effective than those prepared from the cardia, the corpus or the duodenum, according to N. Henning and H Brugsch (Deut med Wchnschr 57 757 (May 1) 1931)

Seven to 10 Gm ( $1\frac{3}{4}$  to  $2\frac{1}{2}$  drams) of desiccated, defatted, whole **hog stomach** daily is effective, according to C C Sturgis and R Isaacs (Am J M Sc 180 597 (Nov.) 1930), in inducing and maintaining a hemopoietic remission in patients with pernicious anemia. This amount represents from 50 to 67 Gm ( $1\frac{2}{3}$  to  $2\frac{1}{4}$  ounces) of fresh organ. A chemical dosage of 10 Gm ( $2\frac{1}{2}$  drams) for each million red blood cells deficit per c mm is a safe dosage. The response to this substance is similar to that following liver extract. The average increase in the number of red blood cells is 500,000 per c mm per week during the first 8 weeks.

It is hoped that further study of the effects of **ultraviolet rays** in the treatment of pernicious anemia will be stimulated by the report that there has been established for the first time experimental proof that there is a toxic substance in the blood of these patients. This toxic substance is not exhibited in the blood of patients suffering with secondary anemias, leukemia, Hodgkin's disease, carcinoma and other diseases producing an anemic condition of the blood. It is claimed by D I Macht (Brit J Actinotherapy 5 228 (Feb) 1931) that detoxification of the serum

may be obtained by exposure of the serum, in quartz containers, to the rays from the ultraviolet lamp. The duration of the clinical improvement in the patients has not yet been reported, but the results are gratifying so far. In making these phytopharmacologic studies the investigator claims to have evidence supporting the belief that there is present in the spinal fluid this toxin which may throw light on the etiology of spinal lesions that frequently accompany pernicious anemia.

**ANEMIA, SECONDARY.—**  
**ETIOLOGY.**—Secondary anemia is caused by (1) diminished production of erythrocytes and hemoglobin, (2) increased rapidity of erythrocyte and hemoglobin destruction, and (3) blood loss or hemorrhage. It is possible that several of these causes may coexist.

**DIAGNOSIS.**—A. H. Douglas and H. Tannenbaum (Arch Int Med 45: 248 (Feb) 1930) found a low reticulocyte count only in some cases of chronic nephritis and chronic lung abscess, and in some acute infections, particularly acute rheumatic fever. Normal reticulocyte counts were found in 20 cases of secondary anemia without hemorrhage and the authors state that when the output of new red blood cells is diminished, there is a decrease in the number of the younger reticulated cells before there is a corresponding reduction of adult erythrocytes, and, therefore, during the transition from 5,000,000 red blood cells per cubic millimeter to a lower figure, the ratio of reticulated cells to total erythrocytes is below normal. When a new equilibrium is established at a lower figure, the ratio returns to normal, although the total number of both reticulocytes and adult cells is low.

It is, therefore, important, in evaluat-

ing the reticulocyte count in a given case, to know whether the red blood cells are on the increase or decrease. This was emphasized by R. Johnson and H. Berglund (Proc Soc Exper Biol and Med 25: 517 (Apr) 1928).

Increased blood destruction is probably an unusual cause of secondary anemia, since in those conditions in which it is known to occur there is usually a high icteric index, whereas, in secondary anemia the icteric index is usually normal or low, except in certain cases of diseases of the liver or obstruction of the bile ducts.

In secondary anemia due to hemorrhage there is usually encountered a normal icteric index, but an increased percentage of reticulocytes (the normal icteric index is quoted by various authors at from 2.5 to 6). The percentage of reticulocytes following hemorrhage may rise to 35 per cent., according to L. S. P. Davidson and J. G. McCrie (Lancet 2: 1014 (Nov 17) 1928).

**PATHOLOGY.**—The study of all of the anemias has received a great impetus by the discovery of the effect of ingestion of various animal organs, *i.e.*, liver, stomach, kidney, heart, or their extracts, upon the hematopoietic system.

C. S. Keefer and C. S. Yang (Arch Int Med 48: 537 (Oct) 1931) have made a careful study and analysis of 126 cases of anemia in the medical wards of the Peiping Union Medical College, in Peiping, China. Curiously, however, while indicating in their title that all of the cases studied were secondary anemias, aplastic and pernicious anemias were included. They called special attention to changes in the tongue, skin, ocular fundi, nervous system, and gastric analysis. The *tongue* changes consisted of atrophy of the papillae, the degree of which varied from a disappear-

ance from the central portion of the tongue to complete atrophy of all of the papillæ. These changes only lasted during the persistence of the anemias, the papillæ being regenerated and the tongue appearing normal following recovery from the anemia. Other conditions giving this tongue condition without anemia, were found to be recurrent glossitis, sprue, pellagra, and following gastrectomy.

The *skin* changes observed in 2 cases were typical of pellagra and 3 cases exhibited *hyperkeratosis folliculosis*. The latter changes were attributed to deficiency in vitamine A by C. N. Frazier and C. H. Hu (Tr. Int'l Dermat. Conference, Stockholm, 1930).

The changes in the ocular fundi consisted in *retinal hemorrhages*. These occurred only in the very severe forms of secondary anemia, all of them having counts under 1,500,000 cells. Three such cases were due to chronic dysentery and 1 to bleeding hemorrhoids.

The changes in the *nervous system* in secondary anemias occurred only in cases showing gastric anacidity, 2 of which were in cases of chronic dysentery and 1 a case of anemia from hemorrhage. These changes in the nervous system were characteristic of subacute combined degeneration. *Peripheral neuritis* was observed in 2 cases associated with anemia and chronic dysentery, without gastric anacidity, but with nutritional defects, so that it was impossible to rule out beriberi.

The changes in the *gastric secretions* consisted in a transitory absence of free hydrochloric acid.

**TREATMENT** of the 126 cases of anemia varied with the supposed cause. Keefer and Yang (*loc cit*) concluded that the recovery from anemia due to chronic loss of blood may be accelerated

following the administration of **liver** and **iron**. **Blood transfusion** is necessary in the very severe anemias. Sepsis and repeated small hemorrhages slow convalescence. In cases of anemia resulting from lack of vitamins in the diet, treatment is directed toward a **high vitamine diet**, well balanced, and if the anemia is grave or the patient slow to respond, **liver** and **iron** medication.

*Chronic dysentery with anemia* is best treated with **liver extract** and **high vitamine diet**. *Anemia from hook-worm* can be cured with **liver** and **iron**. The *anemias of pregnancy* are variable in their treatment requirements. **iron** or **liver extract** administration or **blood transfusions** may be required.

*Anemia in kala-azar* is difficult to overcome. **Antimony** compounds are used, together with **blood transfusions** and **iron** and **liver extract**. They believe there is great damage to the bone-marrow in this disease which is responsible for the slow recovery from the anemia.

Liver ash is not found valuable in treatment of the various anemias. In some cases of anemia, **liver** and **iron** together are more potent than either when exhibited separately. **Liver** or **liver extract** is most valuable in some *anemias secondary to pregnancy*, in *anemias in undernourished children*, and in the *anemias of chronic dysentery*. It is not always possible, without therapeutic trial, to decide in advance which form of treatment will be most efficacious.

**ANEMIA, VARIOUS FORMS.**  
—**PATHOLOGY.**—The results secured in various cases examined by S. Marino (Pol. Clinica Sez. Med. 37:566 (Dec) 1930), are more worthy of note since not only in experimental anemias,

induced by means of pyridine and tobylenediamine, but also in clinical anemias, the quantitative variations in the *lipoids* and in their relations, as encountered in the blood, point to a disturbance in the lipid equilibrium of the blood. The importance of the relation of the total cholesterol to the phosphatides in researches on anemias emphasized by some authors was not confirmed.

**TREATMENT.**—Since anemia may be caused by various factors, it is essential to decide whether it is a pernicious anemia or hemolytic anemia, in order that the proper treatment may be instituted on the basis of the pathogenesis. The therapeutic methods evaluated by A. Herz (Wien k Wchnschr 43 1189 (Sept 25) 1930) are injection of **hemostatics**, **blood transfusion**, intramuscular injection of **physiological solution of sodium chloride** medication with **iron** or **arsenic** preparations, **liver** or **desiccated stomach** and in some cases **splenectomy**.

**ACHLORHYDRIA AND ANEMIA IN THE AGED.**—One hundred persons over 60 years of age and in normal health were selected and their response to the ordinary fractional gastric analysis recorded by D. T. Davies and T. G. I. James (Lancet 2 899 (Oct 25) 1930). None of the patients had a history of gastric dysfunction. Arteriosclerosis was present in all and the systolic blood-pressure ranged from 120 to 250 mm. of mercury with no apparent relation to the gastric secretion. Achlorhydria cases were treated as a series and their blood findings compared with a like series of patients showing free hydrochloric acid. The condition of the tongue was also noted.

Achlorhydria was present in 32 per cent, low acid secretion in 12 per cent, normal acid secretion in 43 per cent;

and high acid secretion in 13 per cent. A slight degree of anemia was present more frequently in the cases showing true achlorhydria than in those showing a normal amount of acid. Anemia was more common in cases presenting a diminished pepsin secretion than those having a good secretion of pepsin. Atrophic changes in the mucous membranes of the tongue were more frequently associated with achlorhydria than those with a normal secretion.

**ACUTE INFECTIOUS HEMOLYTIC ANEMIA.**—The report of 3 cases of acute infectious hemolytic anemia by M. Lederer (Am J M Sc 179 228 (Feb) 1930) brings the number of cases now recorded in literature to 12. The disease was reported by this writer in 1925, at which time most of the cases had occurred in males. The onset of the disease is characterized by the rapid development of anemia of the icteric type, weakness and increase in temperature, with frequent hemoglobinuria. One-third of the cases have had an enlarged liver and spleen. The blood picture is described as a profound anemia with a high icterus index, leukocytosis and erythroblastemia, *i.e.*, many nucleated red cells. Emphasis is laid upon the presence of megaloblasts, while the platelets are normal in number.

The treatment consists in **transfusion** which promptly brings about the cessation of the hemolytic process. Liver and liver extract have been tried without success.

**HYPOCHROMIC ANEMIA.**—**Treatment.**—The effect of large doses (75 grains—5 Gm., daily) of encapsulated ferrous carbonate was tried by E. S. Mills (Canad M. A J 22: 175 (Feb) 1930), in a group of cases of hypochromic anemia (this term being preferred rather than *idiopathic second-*

any anemia) Only a fair result was obtained The patients were then given iron plus a concentrated form of **vita-  
mine E**, without any appreciable benefit They were then given a capsule contain-  
ing 2 Gm (30 grains) of **ferrous car-  
bonate**, 1.5 mg ( $\frac{1}{40}$  gram) **copper sul-  
phate** and 0.017 Gm ( $\frac{1}{4}$  grain) phenol-  
phthalein, thrice daily The phenol-  
phthalein was added to counteract the  
constipating effect of iron but was  
found to be too laxative and the result-  
ing diarrhea aggravated the anemia In  
the second batch of capsules the phenol-  
phthalein was replaced by **cascara** with  
good results Prompt improvement fol-  
lowed in all cases with restoration of  
the blood to about its normal level

**SICKLE CELL ANEMIA.**—Evi-  
dence is offered by W. Z. Fradkin and  
L. S. Schwartz (Jour Lab Clin Med  
15:519 (Mar) 1930) to the fact that  
most patients with sickle cell anemia are  
susceptible to tuberculosis, probably be-  
cause of their lowered resistance to in-  
fection The diagnosis of an acute sur-  
gical condition in the abdomen of a  
negro patient is hazardous without a  
previous search for sickle cells in the  
blood smear

It was shown by earlier experiments  
that the occurrence of sickle shaping of  
the erythrocyte depended upon oxygen  
tension Experiments conducted by J.  
B. Scliver and T. R. Waugh (Canada  
M. A. J. 23:375 (Sept) 1930) demon-  
strated that in these cases the number of  
sickle cells in the peripheral blood may  
be altered by changes in partial  $O_2$  pres-  
sure, sickling taking place when the  $O_2$   
pressure falls below 45 mm Hg This  
is their explanation of the large number  
of sickle cells in organs examined post-  
mortem Because of the ability of the  
cells to take these unusual shapes in the  
blood-stream and to return to normal

when the  $O_2$  pressure is increased, the  
authors indicate their belief that the  
disease is not primarily one of the spleen  
or the bone-marrow, but that it is due  
to an inherited property of the cells  
which follows the Mendelian law and is  
peculiar to the negro race

### ANEMIA IN CHILDREN.—

The blood and the changes in it brought  
about by disease as it affects the hemato-  
poietic system, either primarily or  
secondarily, vary considerably at differ-  
ent age levels. Normally there is a wide  
variation in the blood picture during in-  
fancy and to a lesser degree during  
childhood

J. M. Baty (New England J. Med.  
203:319 (Aug 14) 1930) reiterates  
the well-known fact that the hemato-  
poietic system of the infant and, to a  
lesser degree, that of the child, is more  
unstable than that of the adult and may  
react in a very bizarre manner to  
stimuli An understanding of anemia as  
it occurs in infancy and childhood is de-  
pendent primarily upon the appreciation  
of this fact

**CLASSIFICATION.**—The follow-  
ing classification of anemia in infants  
and children is offered by Baty, not  
as an inelastic arrangement, but as a  
practical working basis which should be  
useful in diagnosis and treatment—as  
more definite knowledge is revealed the  
classification may be altered

#### Anemia in infants and children

- (A) Associated with primary blood dis-  
turbance
- (B) Associated with neoplasms, parasitic  
infections, chemical poisons
- (C) Associated with so-called primary  
splenomegalies as Banti's disease,  
splenomegaly with gastric hemor-  
rhage, lipoid histiocytosis, Gau-  
cher's disease
- (D) 1 Anemia of prematurity.

- 2 Congenital anemia, such as anemia of newborn, erythroblastic anemia, sickle-cell anemia, hemolytic jaundice
- 3 Dietary anemia
- 4 Anemia associated with infection

Von Jaksch's anemia and pernicious anemia are not included in the classification. For the sake of clarity, as advocated by many authors, Baty considered it advisable to discard the term of von Jaksch's anemia (see Supplement to Sajous's Analytic Cyclopaedia of Practical Medicine, Vol. X, 10th Edit., p. 52). Pernicious anemia, according to Baty (*loc cit*), occurs among the age group under consideration, rarely if ever.

A. C. Hampson and E. C. Warner (Arch. Dis. Childhood 5:299 (Oct) 1930) have divided the anemias of infancy and childhood into the 2 main groups of *hemolytic* and *nonhemolytic*.

(A) Hemolytic anemias

- 1 True pernicious anemia
- 2 Acholuric jaundice
- 3 Hemolytic anemias obviously of infective origin
- 4 Congenital, or occurring in the early months of life

(B) Nonhemolytic anemias

- 1 Anemia due to hemorrhage
- 2 Chlorotic anemias
- 3 Grave secondary (aplastic) anemias.
- 4 Splenic anemia
- 5 Anemias associated with metabolic disturbances.
- 6 Anemias of infective origin
- 7 Anemias associated with Hodgkin's disease, leukemia, chloroma, and glandular fever
- 8 Anemia associated with malignant disease

**FREQUENCY.**—From an analysis of 400 cases, Baty (*loc cit*) found the relative frequency of distribution of the various types of anemia according to his classification to be as follows:

	Cases	Pcr Cent of Total
Group A	52	13
Group B	17	4
Group C	16	4
Group D	315	79
Anemia of prematurity	64	
Congenital anemia	28	
Dietary anemia	30	
Anemia associated with infection	193	
Total	400	

**BLOOD PROPERTIES IN ANEMIA.**—E. M. Mondini (Pediatrics 38:1162 (Nov 1) 1930) made estimations of the fibrin content of the blood-plasma of a group of normal children and of a group with anemia. In normal children the determination of the content of the blood-plasma gave an average of 3.68 Gm per thousand c.c. In the group of anemic children the variation of the fibrin content of the blood depended more on the etiology of the anemia than on the type of the disease. Pseudoleukemia, hypoplastic anemia and kala-azar were associated with hypofibrinemia. The intensity of the hypofibrinemia was in relation to the maximum degree of anemia. The type of anemia secondary to metapneumonic empyema and anemia of the secondary period of tuberculosis were associated with hyperfibrinemia. The content of fibrin in the blood-plasma of patients with anemia caused by purpura hemorrhagica or any other type of post-hemorrhagic anemia was normal. The changes that the fibrin of the blood-plasma undergoes in several types of anemia make the author suspect a probable relationship between the bone-marrow and the formation of fibrinogen.

M. Giuffré (Arch. f. Kinderh. 88:8 (July 12) 1929) studied the relation between the acid-base balance of the



blood and the sedimentation of erythrocytes In 20 infants with anemia, in whom hemoglobin varied between 13 and 56 per cent the  $pH$  was found to be 7.3 or 7.4 by the van Slyke method and in the sedimentation study, there was an increase over normal

*Reticulocytes* in the circulating blood of newly-born infants number approximately 7 per cent, according to C Seyfarth and R. Jurzens (Virchow's Archiv path Anat 266 676, 1928) Following birth, the number decreases rapidly, so that by the sixth week the average count is only 0.7 per cent. In premature infants at birth the reticulocytes are between 10 and 30 per cent, and the percentage decreases more slowly than in normal infants Following the sixth week of extra-uterine life, the reticulocytes are not increased above 1 per cent, except under certain physiologic or pathologic circumstances.

**DIAGNOSIS.**—*Pallor*, according to C. G. Grulee (M Clin. North America, 13.299 (Sept) 1929), must not be confused with anemia. Pallor is a symptom of anemia, but is not anemia. Pallor is due to a decrease in the amount of hemoglobin beneath the surface of the skin While this decrease may be due to anemia, it may also be due to a temporary or sustained contraction of the peripheral vessels

Grulee further pointed out that *hemoglobin* and *red cell* determination not only may be normal but also a definitely high normal and the child may still have anemia Anemia is not determined by blood count, but by *blood volume* and *blood count* in their relations to the body tissue Until better chemical methods are obtained for determining blood volume the fundamental questions of anemia cannot be solved.

**DIETARY ANEMIA.**—This term is variously called nutritional or alimentary anemia, milk or goat's milk anemia Although dietary factors are undoubtedly of importance in the development of anemia in many cases, uncomplicated dietary anemia is relatively rare In general, according to Baty (*loc. cit*) there are 2 important *etiologic factors* in the production of anemia of this type: (1) a deficiency of one or more components necessary to the well-balanced diet, and (2) failure on the part of the individual to utilize properly the ingested food

The *clinical picture* is one of pallor of varying degree, often associated with anoxemia, weakness and irritability. The physical state may remain surprisingly good, but in most cases the muscles eventually become flabby and growth is affected The spleen may or may not be enlarged The erythrocytes range from 1,000,000 to 5,000,000 per c mm The hemoglobin is usually below 60 per cent There is no characteristic change in the leukocytes. Immature cells of all types may be present in large numbers The *diagnosis* rests chiefly on the exclusion of other factors as primary causes in the development of the anemia and in the presence of definite dietary deficiency The diagnosis is made with difficulty in many cases because of the common association of intercurrent infection The *prognosis* in uncomplicated cases is excellent

*Goat's milk anemia*, according to the study made by E. Letterer (Jahrb. f. Kinderh. 130 1 (Dec) 1930), seems to be characterized by a relatively slight regeneration capacity of the blood. If normoblasts are present their number is small, and microscopic examination of the bone-marrow always shows a mod-



erate erythropoiesis. There is a resemblance between goat's milk anemia and pernicious anemia. Letterer believes that the discovery of the constituent of goat's milk that causes anemia will throw light on the question of the pathogenesis of pernicious anemia.

*Anemia in celiac disease*, according to B. Strandquist (Rev. franç. de pédiat. 5:728 (Dec.) 1929) may be due to avitaminosis or faulty absorption from the gastrointestinal tract. The tendency to hemorrhage sometimes observed in these cases may also be dependent upon a lack of vitamin C. In other cases it seems to depend upon certain biologic chemical alterations of the blood plasma. In the latter type the prognosis is particularly poor.

#### ERYTHROBLASTIC ANEMIA.

—Erythroblastic anemia of childhood is a term which has recently been applied by T. B. Cooley to a type of hemolytic anemia which he has separated from the heterogeneous group of so-called von Jaksch's anemia or infantile pseudo-leukemia (See Supplement to Sajous's Analytic Cyclopaedia of Practical Medicine, Vol. x, 10th Ed., p. 52, 1931). While the term seems to be coming rapidly into general usage, A. Capper (Am. J. M. Sc. 181:620 (May) 1931) has objected to its introduction, pointing out that erythroblastosis is a characteristic feature of most of the severe anemias of childhood. The *etiology* is obscure. The disease is characterized by a congenital, familial, and racial incidence, being limited to Mediterranean peoples (Baty *loc. cit.*). A number of cases of erythroblastic anemia have recently been reported (Martha Wollstein and Katherine V. Kreidel, Am. J. Dis. Child. 39:115 (Jan.) 1930; B. R. Whitcher, Am. J. M. Sc. 179:236 (Feb.) 1930).

*Clinically*, the disease is characterized by the Mongoloid facies, due to the muddy, yellowish discoloration of the skin, and a thickening of the cranial bones and the malar eminences. The forehead is high, the eyes are widely set apart, and the lids and epicanthal folds are puffy. The spleen is enlarged. Large numbers of nucleated erythrocytes are found in the peripheral blood.

X-ray studies of these patients reveal a decided thickening of the medullary portion of the cranial bones, with unusually thin inner and outer tables. In the early stages, the marrow is mottled and spongy. In the later stages, a second change is seen in the nature of new bone formation, appearing as striations perpendicular to the tables. The pelvis, spine, ribs, scapulae, and bones of the hands and feet are very porous.

The metacarpals are expanded. The cortex of the long bones is very thin. The medulla is unusually transparent, and within it the trabeculations are sharp and finely penciled with large interspaces. The changes are greatest in the metaphyses, the disease affecting all bones of the body. The bone changes are evidently a reaction of the marrow to prolonged overstimulation, beginning in the cranium before the cortex is firm enough to prevent overgrowth. The striations which later appear in the skull suggest replacement of exhausted marrow by bone. Spontaneous fractures have not occurred. None of these cases show periosteal or joint involvement (R. G. Karshner, Am. J. Roentgenol. 20:433 (Nov.) 1928).

The *prognosis* is not good, the disease running a progressive course (Wollstein and Kreidel, *loc. cit.*).

**GAUCHER'S DISEASE.—Differential Diagnosis.**—According to Kar-

shner (*loc cit*), the bone changes in Gaucher's disease are distinguishable from those occurring in *erythroblastic anemia* by the presence of destructive lesions, joint involvement and periosteal raising, the occurrence of spontaneous fractures, and the absence of skull changes, characteristic of the latter disease. The destructive process in the hip-joint might be indistinguishable from that occurring in the flattened head of the so-called *Legg-Perthé's* type. It should not be confused with tuberculous coxitis. The spinal caries of Gaucher's disease should be easily distinguishable from those of tuberculosis because the intervertebral spaces remain undisturbed.

**HEMOLYTIC ANEMIA.**—S D Lazarus (*Am J Dis Child* 40 1063 (Nov) 1930) described 2 cases of acute hemolytic anemia in children. In reviewing the literature the author could find no direct reference to this entity, although somewhat similar cases were reported. The cause is unknown although an infectious origin has been suggested. The *cardinal symptoms* are a severe, rapid, progressive leukanemia, with signs of approaching coma, air hunger, prostration, high fever, rapid pulse and respiration rates, general hyperesthesia, vomiting, tenderness of the abdomen, and enlargement of the spleen and liver. The *prognosis* seems to be good, as the most striking feature of the entire condition was the rapid recovery after a transfusion of unmodified blood.

**ANEMIA OF THE NEWBORN.**—This very rare condition is apparently a definite clinical entity in which severe anemia is present at birth or develops shortly thereafter. Its cause is unknown. R M Greenthal (*Am J. M. Sc.* 179 66 (Jan) 1930) offers the

conjecture that the true etiologic factor is probably to be found in some temporary defect in the blood-forming tissue of the infant. Three cases of this type of anemia have recently been reported by R M Greenthal (*loc cit*), W M Happ (*Arch Pediat* 47 171 (Mar) 1930) and C F. Gelston and E E Sappington (*Am J Dis Child* 39 807 (Apr) 1930) respectively. The *prognosis* is good, the infant usually permanently recovering at some period during the second half of the first year of life. According to Greenthal (*loc cit*) anemia of the newborn is similar to hemorrhagic disease of the newborn in that the blood defect in each disease is temporary and recovery may occur without treatment.

According to D M Greig (*Edinburgh M J* 36 470 (Aug) 1929), in generalized affections of the bones in conjunction with certain blood diseases, the primary disease lies in the hematopoietic organs (the marrow, or the blood) while the bone affection is secondary. In osteosclerotic anemia, however, the first obvious change is in the bones, and the anemia is secondary to the sclerosis and the centripetal osseous hypertrophy which causes obliteration of the bone-marrow, and its destruction as a blood-forming organ. It is recognized that in certain forms of anemia in which there is disturbance of the splenic function or when the spleen has been removed, there occurs a compensatory overgrowth of the red marrow. In osteosclerotic anemia, destruction of the bone-marrow is compensated by a recrudescence of the hematopoietic function of the spleen and to a less extent of the liver, both these organs undergoing enlargement.

Greig reported a case of osteosclerotic anemia in a boy 11 years of age, ad-

mitted to the hospital with a diagnosis of idiocy due to some congenital cerebral defect, and rachitic anemia. No treatment brought improvement. The anemia became more intense, his spleen and liver increased in size, and some months later the child died of a progressive general asthenia. In addition to presenting an excellent description of the skull, Greig pointed out that while skull changes in osteosclerotic anemia may be congenital, the microcephaly is resultant and acquired. In congenital microcephaly the brain is at fault, while in osteosclerotic anemia the skull is at fault, interfering with the development of the brain.

**PERNICIOUS ANEMIA.**—This disease is so rarely observed in infancy and childhood that it is often questioned whether it ever occurs during this period of life (Baty *loc cit*). W. W. Anderson (Am J Dis Child. 39: 233 (Jan) 1930) reported a case in a child 8 years of age and K. W. Anderson (Minnesota Med 13: 297 (May) 1930) reported 2 cases in young girls, aged 15 and 18 years respectively. Hampson and Warner (*loc cit*) have observed 4 cases of this pernicious type of anemia, 2 of which they report in detail, in infants 4 months and 8 months of age respectively. In all 4 cases the onset was very sudden; recovery was rapid following suitable treatment.

**ANEMIA OF PREMATURITY.**—According to Baty (*loc cit*), anemia of prematurity is a physiologic change. At birth the blood of premature infants is comparable to that of full-term babies. In premature infants there is a rapid fall in the number of erythrocytes and in the hemoglobin percentage during the first few weeks of life, the lowest values being reached by the end of the third month. The degree of the ensuing

anemia is inversely proportional to the duration of the pregnancy, the red blood-cells commonly numbering 2,500,000 to 3,000,000 per cmm and the hemoglobin 45 to 55 per cent. There is then a gradual increase in the erythrocytes and hemoglobin until at the sixth or seventh month of life, when the values are again comparable to those in the full-term infant.

**Etiology.**—One explanation for the development of this physiologic anemia is that the storage of iron, which is thought to be accumulated in the liver during the last 3 months of fetal life, is insufficient in the prematurely-born infant and becomes exhausted before iron-containing foods are added to the diet. P. Silberschmidt (Jahrb f. Kinderh 129: 63 (Sept) 1930), however, states that the anemia is apparently not due to iron deficiency, for iron administered therapeutically is not utilized. Another theory, according to Baty, is that the premature infant is unable to utilize iron properly.

**Symptomatology.**—Anemia of the premature infant is evidenced clinically by pallor of the skin and mucous membranes and, as a rule, is unaccompanied by cessation of gain in weight and height. The spleen may or may not be enlarged. Evidences of increased hemolysis or of loss of blood do not appear.

**SICKLE-CELL ANEMIA.**—The term *sickle-cell anemia* should not be confused with *latent* or *active sickle-cell anemia*. *Latent sickle-cell anemia* seems to represent the period of remission of the disease, and *active sickle-cell anemia*, that of exacerbation. The term "*sickle-cell anemia*," or the sickle-cell trait, should be reserved for those cases in which blood preparations on standing for from several to 24 hours show sickle erythrocytes, while the health of the persons

affected is apparently normal—their blood being without other abnormalities, and their previous history being free of symptoms and signs of sickle-cell anemia (B Steinberg, Arch Path, 9 876 (Apr) 1930)

The cause of sickle-cell anemia is unknown. Jessie Scriver and T R Waugh (Canad M A J 23 375 (Sept) 1930, Am J Dis Child, 40 922 (Oct) 1930) agree with certain other observers that the ability of the cells to “sickle” is probably not due to the disease of the spleen or bone-marrow, but rather to an inherent property of the red blood-cells which follows the Mendelian law and is peculiar to the negro race. These authors determined the correlation between gaseous changes in the blood and the phenomenon of sickling. Blood was obtained from the antecubital vein. It was first taken without applying the Esmarch bandage. Fifteen to 20 per cent of the cells in wet sealed preparations were found to be sickled. Ninety-five per cent of the cells were found sickled when the specimen of blood was obtained after marked stasis was produced by means of a tight Esmarch bandage. However, only 5 to 10 per cent of the cells were sickled when the blood specimen was obtained after friction had been applied and the arm immersed in hot water in order to produce maximum oxygenation. The carbon dioxide and oxygen contents were determined on the blood samples. An oxygen dissociation curve of the blood was also obtained, and this presented a shift to the right, as is seen in severe anemia, but the type of curve was essentially normal. The curve was plotted to show in millimeters of mercury the relationship of the oxygen pressure to the percentage of sickle-cells. A definite change was seen with in-

creased sickling around a pressure of 40 mm of mercury. These results corroborate the *in vitro* observations of E V Hahn and Elizabeth B Gillespie (Arch Int Med 39 233 (Feb) 1927), who showed that sickling took place when the partial oxygen pressure fell below 45 mm of mercury.

**Pathology.**—B Steinberg (*loc cit*), from an analysis and summary of the necropsy findings reported, and from those of his own cases, has pointed out that single and multiple *ulcers of the leg* are commonly present in sickle-cell anemia. The left side of the *heart*, and particularly the ventricular wall is often moderately hypertrophied. The myocardium is frequently observed to have slight to moderate patchy, fatty degeneration. The *spleen* is either enlarged or atrophied, apparently enlargement occurs with exacerbation of the anemia in the first 4 years of life, while in older patients atrophy is the rule. A R Rich (Bull Johns Hopkins Hosp 43 398 (Dec) 1928) found an abnormal development of the follicular capillaries and a malformation of the sinuses around the follicles, with the presence of pools of blood in the pulp about the Malpighian bodies—changes pathognomonic of sickle-cell anemia. The *liver* is moderately enlarged, with an associated infiltration of round cells in the periportal spaces and occasionally in the lobules. The external surface of the *kidneys* is finely and irregularly scarred, with an occasional large scar occurring. The glomeruli are large and red. In the *bones*, sclerosis of the cortex and the marrow cavity is observed at both ends of the bones, with a central red marrow beneath the leg ulcer. Elsewhere in the long bones, the inner half of a generally thickened cortex contains islands of hyperplastic marrow and areas of necrosis.

and intramembranous bone repair. Practically similar changes are observed in the bones of the skull and ribs. Early in the disease, x-ray examination reveals a porous appearance of the bones, while in the terminal stage, striations occur. The mucosa of the *stomach* and the *ileum* contains a small number of polymorphonuclear neutrophils.

**Prognosis.**—The disease seems to be more serious in the child than in the adult. According to W. M. Yates and M. Mollari (J. A. M. A. 96:1671 (May 16) 1931), relatively few persons develop the active phase of sickle-cell anemia, where the sickling takes place in the circulating blood and severe anemia results. Those who do develop it die before the age of 30 years. Persons with the sickle-cell anemia have lived to old age without any apparent disturbance to health. The prevailing conception is that sickle-cell anemia *per se* is not fatal but that a patient with it and some intercurrent disease is more apt to succumb to the secondary condition. Nevertheless, patients with sickle-cell anemia may die as a direct result of the anemia. W. C. Cook (J. Med. 11:541 (Dec) 1930) reported a fatal case in a negro boy, 7 years of age. Necropsy examination revealed subarachnoid hemorrhage with cerebral softening and a generalized thymo-lymphatic hypertrophy. Yates and Mollari (*loc cit*) observed an adult who died with sickle-cell anemia during an abdominal crisis, death apparently being due to an arterial thrombosis of the liver.

**Treatment of Various Forms.**—**Blood Transfusion.**—Blood transfusion, according to L. Krahulik and L. A. Koch (Am. J. Dis. Child. 39:34 (Jan) 1930), is a most valuable therapeutic agent when used in various nutritional disorders complicated by anemia. As a

rule, in nutritional anemia, W. W. Anderson (Arch. Pediat. 47:707 (Nov) 1930) recommends blood transfusion when the hemoglobin determination is below 50 per cent. Baty (*loc cit*), as well as Anderson, is of the opinion that small, repeated transfusions apparently give better results than larger ones. In cases of anemia where liver therapy has been adapted, A. C. Hampson and E. C. Warner (*loc cit*) sometimes find it necessary to give an initial transfusion. These authors, as well as Baty, consider blood transfusion of great value in severe cases of hemolytic anemia. Blood transfusion seems to be particularly valuable in the treatment of *anemia of the newborn*. C. F. Gelson and E. E. Saffington (*loc cit*), R. M. Greenthal (*loc cit*).

In the treatment of *aplastic anemia* blood transfusion is unsatisfactory. G. Abraham (Arch. f. Kinderh. 90:161 (May 24) 1930, also J. H. Root (New England J. Med. 203:1225 (Dec 18) 1930). Hampson and Warner (*loc cit*) state that not only do blood transfusions appear to exert very little influence on the course of this disease, but that in some cases they appear to lead to an exacerbation of the condition. Birk (Munchen med. Wchnschr. 77:575 (Apr 4) 1930), however, reported successful treatment of a case of *aplastic anemia* by means of blood transfusion. In order to restore the function of the bone-marrow, Birk gave repeated transfusions, 40 in all. Other treatment consisted of iron and arsenic by mouth and a diet including raw vegetables, liver, fruit juices and bone-marrow.

**Iron.**—H. W. Josephs (Southern M. J. 23:1135 (Dec) 1930) felt that medicinal iron given in sufficiently large amounts has a greater effect in raising

hemoglobin than does food iron, and Hampson and Warner (*loc cit*) found **iron ammonium citrate** the best form in which to administer it

C G Grulee and H N Sanford (Am J Dis Child 41 53 (Jan) 1931) in the treatment of anemia, injected colloidal iron (as ferric hydroxide) intraperitoneally. Five c.c. (80 minims) of the solution containing 8 mg ( $\frac{1}{8}$  grain) of colloidal iron was used twice a week for 8 doses. These injections, combined with **ultraviolet light** or with 1 or 2 **transfusions** of blood, seemed to be of value in the treatment of children with *secondary anemia*. It apparently had no effect on the hemoglobin or red cells in primary anemia.

According to F S Robschert-Robbins and G H Whipple (Am J Physiol 92 400 (Mar) 1930), spinach and cabbage produce but a moderate effect on hemoglobin regeneration in standard anemia experiments. Iron in optimum dosage added to the spinach ration may give complete summation, that is, the total effect as a rule will amount to the moderate spinach effect plus the iron salt effect. W W Weston (J. A. M. A 95 834 (Sept 20) 1930) recommended that the mineral elements of the milk be improved by adding spinach concentrate, lettuce concentrate or carrot-top concentrate in suitable proportions to all milk, regardless of the baby's age, if the hemoglobin is below 75 per cent. According to the author, carrot-top concentrate and lettuce concentrate possess an equal and under certain circumstances a superior food value to spinach concentrate. Spinach and apparently carrot-top and lettuce concentrates are useful as reliable sources of *iodine, manganese, iron and copper*.

**Copper**—According to J Waddel, H Steenbock and E B Hart (J Biol

Chem 83 243 (July), 84 115 (Oct) 1929), a fine iron salt, when fed in large amount, does not seem to correct the anemia induced in young rats by a milk diet. However, when copper is added in one form or another recovery takes place. As a result of the work of Steenbock and his collaborators, E Schiff, H Eliasberg and N Joffe (K Wchnschr 9 2144 (Nov 15) 1930) instituted copper therapy in the treatment of 4 anemic patients. In 2 of these the anemia accompanied erythrodermia, in 1 it occurred with pylorospasm; and in the fourth, with severe visceral syphilis. Twice daily the infants were given 20 drops of a 1 per cent solution of hydrous copper sulphate, which is equal to almost 5 mg ( $\frac{1}{12}$  grain) of copper daily. Under the influence of this therapy the blood picture improved steadily in all 4 cases.

**Cobalt**—K Waltner (Am J Dis Child 41 1248 (May) 1931) administered a cobalt compound to 21 children with secondary anemia; 14 improved. This metal was also given to 57 undernourished children for 1 month. Thirty-one of the children gained on an average of 250 Gm ( $8\frac{1}{3}$  ounces) weekly.

**Liver Therapy**—J Tuscherer (Monatschr. f. Kinderh 39 264, 1928) obtained definite improvement with liver therapy in a group of children suffering from anemia secondary to infections and alimentary disturbance, improvement, however, did not appear until the third or fourth week of the treatment. Hampson and Warner (*loc cit.*) have found it worth while to try the effect of liver feeding in cases of *hemolytic anemia* occurring in childhood, and J Levy (Ann Int Med. 3 47 (July) 1929) reported marked improvement in 3 active cases of *sickle-cell anemia* when placed on liver therapy. The ingestion



of liver tended to inhibit the formation of sickle cells C M'Neil (Edinburgh M J 37 175 (Oct ) 1930) has found *liver extract* to be of definite value in the treatment of *primary anemia* of the *newborn*

*Liver sausage*, as tested by G H Whipple and F S Robschert-Robbins (Am J Physiol 92 388 (Mar ) 1930) in experimental anemia, showed a moderately high potency for new hemoglobin production which depended upon the amount of liver contained in the sausage, *blood sausage* was also quite effective Liver and blood sausage, according to these authors, deserve careful study as to their applicability to various human anemias *Calf skeletal muscle* (veal) is as effective in hemoglobin production as any skeletal muscle so far tested and is in the class with beef heart *Egg yolks* and *egg white* are relatively inert, *chicken skeletal muscle* (white or dark) is a little less effective than calf muscle *Gelatin* feeding in large amounts will increase somewhat the hemoglobin output above control levels, corresponding to the effect of beef muscle

*Splenectomy* — Splenectomy in pernicious anemia, according to H Hirsch-Kauffmann (Deutsche med Wchnschr 56 1476 (Aug 29) 1930), brings only temporary improvement and in pseudo-leukemic anemia internal therapy brings better results than surgical intervention Martha Wollstein and Katharine Kreidel (Am J Dis Child 39 115 (Jan ) 1930) stated that in familial hemolytic anemia of childhood (erythroblastic anemia of von Jaksch) the prognosis is bad, even though the patient may survive splenectomy for 5 years, the disease is not cured Splenectomy performed on 3 cases of so-called *splenic anemia* reported by S L. Ludbrook

(Arch Dis Childhood 6 239 (Aug ) 1931) appeared not to affect the course of the disease Splenectomy may be indicated as a palliative measure in *Gaucher's disease* in order to relieve certain symptoms such as anemia, purpura with hemorrhages from the mucous membranes, or the pain and discomfort from the heavy viscus D Hunter and W Evans (Proc Roy Soc Med 23 24 (Dec ) 1929) However, the operation must not be looked upon as a curative measure M B Bonta (Arch of Surg 21 851 (Nov ) 1930; H Hirsch-Kauffmann *loc cit*)

Extirpation of the spleen in *Banti's disease* is particularly effective if done during the first stage of the disease E C Warner (Proc Roy Soc Med 23 1405, 1930) successfully treated a patient with advanced Banti's disease by *ligature* of the splenic vein; the patient's condition at the time of operation was considered too serious for splenectomy

*Irradiation* — E C Vogt and L K. Diamond (Am J Roentgenol 23 625 (June) 1930) treated 2 patients with erythroblastic anemia by irradiation over the spleen, there was no evidence of clinical improvement in either patient

**ANESTHESIA.—CHLOROFORM.**—A O Gettler and H. Blume (Arch Path 11·841 (June) 1931) state in a dog killed by the excessive administration of chloroform, the brain contained 551·5 mg of chloroform in 1000 Gm of tissue In animals while fully anesthetized with chloroform the brain contained 270 mg and 284·6 mg in 1000 Gm of tissue. When an animal was in the stage of recovery, the chloroform content of the brain dropped rapidly during the first 34 minutes, so that only 51·3 mg in 1000 Gm. of brain tissue was left From then on, the



chloroform content decreased more slowly, and after 190 minutes there was only 0.16 mg of chloroform present in 1000 Gm of brain. Animals appeared normal again after 40 minutes. At this time they probably had about 45 mg of chloroform in 1000 Gm of brain. From 15 to 30 minutes after the animals appeared normal, the brain contained from 35 to 30 mg of chloroform in 1000 Gm. In the stage of recovery, the lungs contained much less chloroform than the brain.

**Indications.**—H. Hellendall (Zentralbl f Gyn 55 641 (Mar 14) 1931) stresses that in patients with cardiac disturbances, chloroform should not be used even in mixed anesthesia. He has made it a rule to use chloroform only in mixed anesthesia and never to administer more than 5 Gm ( $1\frac{1}{4}$  drams). Because chloroform should be given only when absolutely fresh, he recommends the use of ampoules containing only 5 Gm ( $1\frac{1}{4}$  drams) of chloroform instead of larger containers.

**Syncope.**—*Treatment*—L. Garrelon and G. Pascalis (Presse méd 38 649 (May 14) 1930) state that an **intracardiac injection of epinephrin** is of great value in syncope caused by ether, ethyl chloride and spinal anesthesia and in *primary chloroform syncope*, but that it is inevitably fatal in secondary chloroform syncope. On the basis of experiments, the authors state that in the *secondary form* of chloroform intoxication, **intracardiac injections of atropine** have a definite curative action on the heart arrested by the anesthetic. Since only 0.5 mg ( $\frac{1}{120}$  grain) of atropine is required to paralyze the inhibition system of the heart, not more than this amount should be used.

**COLONIC ANESTHESIA.**—J. T. Gwathmey (J. A. M. A 93 447

(Aug 10) 1929) reports his experience of 5000 cases anesthetized by the introduction into the colon of **ether in olive oil**. Experiments on animals have shown that if 0.01 Gm ( $\frac{1}{6}$  grain) of **morphine sulphate** per kilogram ( $2\frac{1}{2}$  pounds) of body weight is given previously, full surgical anesthesia can always be assured, it is completely controllable if the correct dose is administered and can be promptly terminated by lavage. Colitis is unknown where no previous inflammation has existed. The special advantages of the method are that there is no psychic shock, less bleeding than with ordinary anesthesia, and the recovery is uneventful, without nausea. The ether is really outside the body until it evaporates and is absorbed. Gwathmey gives charts showing the evaporation rate. He does not consider renal, pulmonary, or cardiac conditions *contraindicate* its employment, but all pathological conditions of the lower bowel, including colitis, hemorrhoids, and fistula, should bar its use. Special *indications* for the method are alcoholism, obesity, brain surgery, esophagoscopy, suspension laryngoscopy, bronchoscopy, hyperthyroidism, and operations on the head, neck, and chest. During colonic anesthesia the pulse rate, respiratory rate, and blood-pressure are said to be lower than under ordinary conditions.

*Control* of anesthesia during the operation can be effected by placing a towel over the face to ensure rebreathing; the occasional use of supplementary open anesthesia; and the introduction into the rectum of a further dose of 65 to 75 per cent ether in oil, about 1 ounce (30 cc) for each extra hour of anesthesia required.

**Technic.**—The night before the operation a light supper of tea and toast

is given, followed after 2 hours by 2 tap-water enemata with an interval of 20 minutes between them, and the administration of 10 grains (0.65 Gm) of barbitol. Two hours before the operation a low clear-water enema is given, and  $\frac{1}{8}$  grain (0.008 Gm) of morphine sulphate is injected intramuscularly, a 10 grain (0.65 Gm) chlorbutanol suppository is inserted deeply, and  $\frac{1}{2}$  hour later an injection of atropine  $\frac{1}{150}$  grain (0.0004 Gm) is given. Rectal instillation of the "retention enema" is then begun, the catheter and funnel being first filled with warm oil to exclude air, the retention enema mixtures in use are: ether 4 ounces (120 cc), olive oil 2 ounces (60 cc), paraldehyde 2 drams (8 Gm), or ether 5 ounces (150 cc), oil  $2\frac{1}{2}$  ounces (75 cc), paraldehyde 2 drams (8 Gm), or ether 6 ounces (130 cc), oil 3 ounces (90 cc), paraldehyde 2 drams (8 Gm). Forty minutes before operation a final enema is given consisting of ether 3 ounces (90 cc) and olive oil  $1\frac{1}{2}$  ounces (45 cc), 10 minutes being taken for its administration; absolute quiet must then be assured for the patient. *Danger signals* are cyanosis, dulled corneal reflex, and stertor; *support of the lower jaw* will usually correct the last-named.

Summarizing his results, Gwathmey states that 65 to 75 per cent ether in oil is nonirritating; the method can be used with safety where a cautery is to be applied in the region of the mouth; there is an absence of any "pain reflex" when the patient recovers; and sometimes there is actual amnesia of the fact of operation.

W. Wood (Brit. M. J. 2: 1155 (Dec 21) 1929; Anesth. and Analg. 9: 123 (May-June) 1930) finds that for long anesthesia, rectal ether-oil anesthesia,

has less ill-effects than any other type. In 50 administrations for *brain operations* he had 1 case of irritation with slight hemorrhage.

**ETHYLENE.**—According to P. D. Woodbridge (New England J. Med. 205: 712 (Oct 8) 1931), although a few instances have come to his attention in which hospitals previously using ethylene have given it up, yet it is his impression that almost all anesthetists who have used it extensively in the past are continuing its frequent use. The author quotes Nix, of New Orleans, who sent out a questionnaire concerning ethylene to all parts of the country. The replies covered 100,000 administrations. Among these there occurred not one immediate death, and but 2 that might indirectly be due to ethylene. He feels that its use is growing, and that it is particularly adapted to the humid climate of the south.

Attempts to demonstrate a reversible combination between ethylene and hemoglobin were made by R. D. Barnard and A. B. Hastings (Anesth. and Analg. 9: 234 (Sept.-Oct.) 1930). They use 3 methods: (1) gasometric; (2) electrometric, and (3) spectrophotometric. No evidence of such a combination was found, and the conclusion seems justified that ethylene does not enter into any combination with hemoglobin.

**Ethylene Explosions.**—According to Woodbridge (*loc. cit.*), explosions of ethylene have been given greater publicity than those of ether. So far as the author is aware, there have been but 4 deaths from ethylene explosions. In the light of present knowledge all these deaths would be preventable. Regarded from the point of view of explosion, it appears to be an extremely safe anesthetic.

A report from the United States Bureau of Mines (Anesth and Analg. 9 6 (Jan-Feb) 1930) points out that in testing the explosibility of varying mixtures of gases, the results depend on several variable factors. With the standard technic of the Bureau, ethylene is inflammable in mixtures of from 3 to 80 per cent with oxygen. The mixtures commonly used for complete surgical anesthesia, therefore, appear to be nonexplosive, although by altering conditions, mixtures up to 80 per cent ethylene can be made to propagate flame.

The report of the Committee on Anesthesia Accidents of the American Medical Association (J A M A 94. 1491 (May 10) 1930) reviews the answers to questionnaires covering about 640,000 ethylene anesthetics, and makes further recommendations. Gas tanks not recently tested for pressure tolerance should not be used. No oil should be used on the valves of oxygen or nitrous oxide tanks. All electrical apparatus in the operating room should be so enclosed as to be gas proof. They agree that high relative humidity is good protection from static spark arising outside the gas machine, but feel that better protection is afforded by complete grounding of the operating room floor, furniture, and personnel. The mere grounding of the gas machine to a water pipe is probably ineffectual.

H B Williams (J A M A 94. 918 (Mar 29) 1930), reporting for the Committee of the Physical Therapy Council of the American Medical Association upon the possibility of explosion of ethylene and other combustible gases used in inducing anesthesia, considers that there is a real danger where ethylene or ether vapor is mixed with oxygen or nitrous oxide and contained

in, or passed through, rubber bags and tubing, the risk is increased by the practice of washing out the apparatus with oxygen-rich mixtures, and administering these to the patient. Although every care may be taken when the cautery is used, the fact that the mixture in the patient's lungs and upper air passages may become explosive by mingling with respired air is liable to be overlooked and may result in a disaster. Less obvious causes of ignition are the electric sparks which may result from the re-establishment of electrical equilibrium after charges have accumulated, in consequence of friction upon some insulated rubber portion of the apparatus. Experimentally, sufficient voltages to cause an explosion were obtained under favorable circumstances by friction of rubber surfaces against each other, though the spark was quite small and almost noiseless. The remedy advocated is the elimination of rubber, the equipment being made conductive throughout. Williams remarks that *ethylene*, being more dangerous in this respect than ether, *should never be used for operations with the cautery or diathermy apparatus, ether should never be employed in any throat operation with such instruments*. Care should also be taken not to comb or stroke the patient's hair until the ethylene has become thoroughly dissipated. The majority of explosions with ethylene were bound to occur towards the end of the operation, and this, according to Williams, may be due to the practice of washing out the patient's lungs with a mixture of oxygen and carbon dioxide.

**PERCAINE.**—As the result of his own observations, H Bruchholz (Deutsche Ztschr f Chir 223:202 (Mar) 1930), and a study of over 4000 cases reported in the literature, comes

to the conclusion that percaine, which is the hydrochlorate of butyl-oxyquinolin-carbonic acid diethylaminoethylamide, is an entirely nonirritant local anesthetic which, experimentally and clinically, is far superior to cocaine and the derivatives of cocaine hitherto employed, both in efficiency and the duration of its action. It can be used for infiltration conduction and surface anesthesia, as well as for the local treatment of **painful wounds and ulcers** in place of anesthesin and anesthesiform. For infiltration anesthesia a 0.5-1000 solution, and for conduction anesthesia a 1-1000 solution, are required. When used in a strength of 1 to 2 per cent, percaine acts as well as a 10 to 20 per cent solution of cocaine, and its action lasts considerably longer; while in a 1 per cent solution it is far superior to alypin, psicaine, and other cocaine derivatives for **anesthesia of the urethra and bladder**. The special practical advantages of percaine are the simplicity of its preparation, its durability, and the readiness with which it can be sterilized, as well as its cheapness. In spite of its relatively high toxicity, it can safely be used in the dilution and doses stated. It is preferably injected *in combination with suprarenin* in doses of 400 c.c. ( $13\frac{1}{3}$  ounces) of a 1-2000 solution, 150 c.c. (5 ounces) of a 1-1000 solution, or 50 c.c. ( $1\frac{2}{3}$  ounces) of a 1-500 solution. The maximal dose is about 0.2 Gm. (3 grains) percaine. It is only in operations on the head, neck, and genital region that smaller doses should be used (up to 0.1 Gm.— $1\frac{1}{2}$  grains—percaine) and, if possible, in combination with *adrenalin*. Percaine is also suitable for **lumbar anesthesia**, but further experiments are required to determine the optimal dose for this purpose.

H. Doench (Zentralbl. f. Chir. 57:518 (Mar. 1) 1930) who has employed percaine in about 130 cases, including operations for **hernias, tumors, hydroceles, appendicectomies, peritonitis, pancreatitis, artificial anus, bursitis**, etc., states that the chief objection to percaine lies in the long time (6 to 10 minutes) it takes to produce complete anesthesia, but this is counterbalanced by the great advantage of its protracted action (6 to 14 hours). No toxic symptoms of any kind were observed.

**Use in Otorhinology.**—() Boserup (Ugeskr. f. læger 92:411 (Apr. 24) 1930) from the Finsen Institute, in Denmark, reports investigations made for over half a year with percaine (Ciba). For surface anesthesia a 2 per cent solution was used, for infiltration anesthesia a 0.2 per cent, and later a 0.1 per cent solution was employed, the action of the last-named solution proving satisfactory. At first a 0.1 per cent solution of adrenalin was added (9 drops to 50 c.c.— $1\frac{2}{3}$  ounces—of the solution), but it was soon dispensed with in order that the action of the percaine might be better studied. Dispensing with the adrenalin entailed more bleeding, but there was no demonstrable reduction of the anesthetic action of the percaine. It was tried on 93 occasions, on 15 of which it was used for **surface anesthesia** during examinations of the **larynx**, for **excisions**, for **galvanocauterization**, and for the application of radium. On 44 occasions it was employed for surface anesthesia for **turbinectomies** and the **removal of polypi**, and in 12 cases for infiltration anesthesia for **tonsillectomy**. The patients' ages ranged from 14 to 61 years, and the amount of the 0.1 per cent. solution used was—in a case of **laryngofissure**, for example, between 30 and

35 c c (1 to 1½ ounce) About 25 c c (5⁄8 ounce) was required for an **antrum resection**, 20 c c (2⁄3 ounce), for a tonsillectomy in an adult, and 10 to 15 c c (1⁄3 to 1⁄2 ounce) for the same operation in children In no case were any signs of poisoning observed, the healing of the operation wounds ran a normal course, and there was no evidence of injury to the tissues Anesthesia was rapidly induced, it was complete and remarkably persistent, so much so that postoperative pain was in most cases not felt. Paresthesias and hyperesthesias seemed to be less marked than after novocaine-adrenalin anesthesia

**Untoward Effects.**—H Florcken (Zentralbl f Chir 57:874 (Apr 5) 1930), commenting on a recent paper by W Brandesky, who drew attention to the *persistent vomiting* and deep *necrosis of the skin* following percaïne anesthesia, states that in his experience of about 400 cases he has never had any complications of this kind He attributes the occurrence of *toxic vomiting* to the fact that Brandesky did not add any adrenalin to his solutions Percaine without adrenalin causes first a transient local hyperemia, which is then followed by a certain degree of anemia The toxic vomiting is probably due to too rapid absorption The occurrence of *skin necrosis* is more difficult to explain and is probably due to local infection not connected with the anesthetic. In the numerous cases in which Florcken has used percaïne he has never seen any necrosis of the skin and has, therefore, no reason to abandon its use as Brandesky has done, especially since it possesses the inestimable advantage of outlasting the period of pain caused by the wound In his hands it has been satisfactory He regards it as essential not to exceed a dilution of 1 1000 and al-

ways to add 1 or 2 drops of a 1 1000 adrenalin solution

According to P D Woodbridge (*loc cit*), percaïne has not gained popularity in this country because of its apparent toxic or irritant effects E L Keyes and A M McLellan (Am J Surg 9 1 (July) 1930), however, prefer it to procaine and report its use in 100 **urological cases**. Length of the anesthesia was 7 hours They refer to 3 previously reported deaths after the subcutaneous administration of 90 and 130 c c (3 to 4½ ounces) of 1·1000 solution and after an intradural injection that was intended to be paravertebral. They also report 5 previously unpublished deaths, 3 of which followed the injection of strong solutions by mistake, 1 followed the subcutaneous injection of 380 c c (12½ ounces) of 1 1000 solution, and the fifth followed the injection of 1 per cent solution into the bladder

**NITROUS OXIDE.**—*Technic.*—A technic for nasal administration of nitrous oxide for **tonsillectomy** which it is claimed abolishes all danger of inspiration of blood, etc., is described by C B Hollis, J V F Clay and H S Ruth (Anesth and Analg. 9:49 (Mar-Apr) 1930) Their claim is proved by postoperative laryngoscopic examinations The patient sits in a chair, leaning forward The surgeon's head is below that of the patient, so that he looks slightly upward into the field of operation The method is easy for the anesthesiologist, abolishes the danger of inspiration, and by affording a clearer field of operation for the surgeon, results in a lessening of the proportion of incomplete operations

**Results.**—E. Jeckl (Schmerz Narkose-Anesth 2:289 (Nov 15) 1929) records his observations on 184 cases in

Professor Hans Finsterer's surgical clinic in Vienna, in which nitrous oxide was used as an anesthetic. He believes that owing to its lack of toxicity and the absence of any injurious effects to any organ, nitrous oxide anesthesia can be employed even in patients who could not tolerate another general anesthetic owing to disease of the lungs, heart, vessels or other organs. Its field of application can be extended by combining it with local anesthesia. The only risk of nitrous oxide anesthesia consists in cyanosis, which can be avoided by an experienced anesthetist and the use of a good apparatus.

D von Klimbó (Arch. f. klin. Chir. 161:259 (Aug 26) 1930) prefers this anesthesia to any other. He has employed it in more than 300 cases, including laparotomies, done for various reasons, even a resection of the stomach, amputation of an extremity, herniotomy and cholecystectomy. He states that it has many advantages over general anesthesia: it is given easily, the patient does not mind taking it, he awakens quickly afterward and has fewer postanesthetic discomforts; it has no bad effects on the air passages or viscera in general. Postanesthetic bronchitis and pneumonia are exceedingly uncommon. However, the anesthesia is not sufficiently deep for laparotomies and it is more expensive than other means of anesthesia.

**INTRAVENOUS ANESTHESIA.—Alcohol.**—A favorable report by Marin (Arch. internat. de laryng 244 (Feb.) 1930) and another by J. D. Constantin (Lancet 1:1393 (June 28) 1930) of over 40 intravenous alcohol administrations is contradicted nearly point by point by R. Palma (Riforma med. 46:513 (Apr. 7) 1930), who finds that thrombosis of the vein is almost

constant, and marked lowering of the blood-pressure, pulmonary congestion, and renal lesions are frequent.

**INTRATRACHEAL ANESTHESIA.**—W. Woodbridge (New England Med 205:712 (Oct 8) 1931) believes that intratracheal anesthesia, popular in Canada, is gaining ground in this country, encroaching on the fields of nasal, pharyngeal, and rectal administration. I. W. Magill (Brit. M. J. 2:817 (Nov. 15) 1930) states that the fundamental principle of endotracheal anesthesia is the provision by intubation of an airway that is proof against obstruction. High-pressure insufflation is usually unnecessary. Deep anesthesia is not essential for intubation. Dexterity in intubation minimizes the disadvantages. Owing to the greater ease with which intubation can be performed through the nose, this route should always be chosen when possible.

**LOCAL ANESTHESIA.**—C. O. Rice (Anesth. and Analg. 9:76 (Mar.-Apr.) 1930) reported on the use of local anesthesia for the reduction of fractures. His review of the literature indicates that the method is used extensively, one author reporting over 2000 injections. One per cent. *procaine-epinephrin* solution is injected into the fracture gap. In case anesthesia does not develop within 3 or 4 minutes, a ring of periosteum of the proximal fragment should be injected in addition. He gives detailed instructions for the injection of the more common fractures. Contraindications are infection and compound fracture. In 200 cases he has met with no complications, and none have been reported by others. It does not result in infection or in delay in healing.

A. Fryszman (Ztschr. f. Urol. 24:646, 1930) announces a novel method of



anesthetizing the male urethra prior to instrumentation. A suppository of *oil of theobroma* 6 cm long and 4 mm in diameter, containing 0.3 Gm (5 grains) of *procaine hydrochloride* is introduced and massaged toward the posterior urethra. It should be placed in warm water before insertion, and 20 minutes should be allowed for anesthesia to develop.

**INTRAVENOUS LOCAL ANESTHESIA.**—For the last 5 or 6 years, J. T. Morrison (Brit. J. Surg. 18: 641 (Apr.) 1931) has used a method of intravenous local anesthesia that calls for the use of 1 tourniquet and 1 needle puncture only. No time is spent on isolating a segment of a limb. The whole limb distal to the tourniquet is dealt with. There is no advantage in trying to limit the area of anesthesia and, as a matter of fact, it is not possible to do so even by Bier's technic. By means of an elastic bandage or thoroughly padded tourniquet of caliber suited to the bulk of the limb, the arterial circulation is arrested at a convenient level in the arm or the thigh. Pressure should be applied slowly so as to insure distention of the veins. With a fine needle on a Record syringe a superficial vein is entered and a quantity of *procaine hydrochloride* solution injected. The injection is usually made in the distal direction. A pad and bandage are applied to prevent possible leakage into the tissues. The amount used has varied from 6 c.c. (1½ drams) of 2 per cent to 12 c.c. (3 drams) of 3 per cent solution, according to the size of the limb to be anesthetized. The method has so far only been employed in adults. The 6 c.c. of 2 per cent was definitely too small a dose, but 10 or 12 c.c. (2½ to 3 drams) of 2 per cent is perfectly successful in dealing with an upper limb.

The patient in whom the maximum dose was given, 12 c.c. (3 drams) of 3 per cent, was a well developed, though elderly man, with a **compound fracture dislocation of the ankle**. The injection was made into the dorsal venous arch on the foot and the tourniquet applied above the knee. In about 8 minutes the sensation is sufficiently abolished in the deeper parts of the limb to permit of operative intervention. Anesthesia of the skin, however, may not be complete. If this is so, the line of the incision may rapidly be infiltrated subcutaneously with 0.5 per cent *procaine hydrochloride* and operation be proceeded with at once. When fully established, anesthesia is absolutely perfect so that even wrenching and dislocating movements give no pain. When the operation is over—but never in less than half an hour after the injection of the anesthetic—the tourniquet is slowly released so that blood from the limb reaches the general circulation only gradually.

In the cases in which the author has employed intravenous local anesthesia it has usually been the fear of chest complications in tuberculous subjects that has led to its use. It has also been useful in elderly patients suffering from shock, although in the presence of advanced arterial disease the use of the tourniquet might perhaps be viewed with concern. There can be no doubt that for one working single-handed it would be invaluable in dealing with **lacerations, fractures, or dislocations of the extremities**, on account of its simplicity, certainty and safety. It is not suggested that in the lower limb it should replace spinal anesthesia, but even there occasions do arise when the necessary solution and a suitable needle are not available for the latter technic.



**REGIONAL ANESTHESIA.**—G. Labat (Surg Gynec Obst 50 74 (Jan) 1930) described the induction of paravertebral alcoholic nerve block for the relief of **pain following thoracoplasty**, and J C White (Am J Surg 9 98 (July) 1930) made a further favorable report on the use of the same method in treating **angina pectoris**. P D Woodbridge (Am J Surg 9 278 (Aug) 1930) reviewed various therapeutic uses of regional anesthesia, including the treatment of **reflex anuria, sciatica, ileus and tetanus**, and the relief of pain in **carcinoma, tuberculous laryngitis, and diseases of the thoracic and abdominal viscera**. The treatment of **ileus** by splanchnic anesthesia is advocated by A Ochsner, I M Gage, and R A Cutting (Anesth and Analg 9.91 (Mar-Apr) 1930, Arch Surg 20.802 (May) 1930).

**THERAPY.**—According to P D Woodbridge (New England Med 205 712 (Oct 8) 1931), methods used in anesthesia are being used more and more in therapy and the services of the anesthetist are thus coming into wider activity outside of the preparation of patients for operation.

**Carbon Dioxide Inhalation.**—Y Henderson, H W Haggard, P N Coryllos, and G L Birnbaum (Arch Int. Med 45.72 (Jan) 1930) and Y Henderson and H W. Haggard (J. A M A 94 2001 (June 21) 1930) have pioneered in the use of this procedure, urging its adoption for the prevention of **postoperative pneumonia** and in the treatment of **carbon monoxide poisoning, atelectasis of the newborn, and if taken early, medical pneumonia**. Henderson has properly ridiculed the medical profession for permitting the maternity hospital to send for the city fire department to resuscitate

their newborn instead of developing their own gas therapy.

C K Drinker and T J Shaughnessy (J Indust Hyg 11 301 (Nov) 1929) advise starting the treatment of carbon monoxide poisoning with 7 per cent carbon dioxide in oxygen, and shifting later to the usual 5 per cent mixture.

Carbon dioxide and oxygen inhalations are being used to bring periods of lucidity to patients with **catatonic dementia precox**. C D Leake, D A Wood, M E Botsford and A E Guedel (Anesth and Analg 9 62 (Mar-Apr) 1930).

**Sodium Amytal.**—W J Bleckwenn (J A M A 95 1168 (Oct 18) 1930, Arch Neurol and Psychiat 24 365 (Aug) 1930) reports most interesting marked therapeutic effects in a variety of severe **neuropsychiatric conditions** from the daily intravenous injection of this drug.

**Rectal Ether.**—According to W A McGee (J A M A 97.922 (Sept 26) 1931), rectal ether is again advised in the treatment of **whooping cough**.

**ANESTHESIA, BASAL.**—P. D. Woodbridge (New England J Med. 205 712 (Oct 8) 1931) defines this phrase as used to indicate so deep a state of narcosis produced by preliminary medication that the amount of added inhalation anesthetic required to produce surgical anesthesia is greatly reduced and the patient is unaware of its administration. Various derivatives of barbituric acid may be used either as simple preliminary hypnotics or as basal anesthetics.

**SODIUM AMYTAL.**—The large number of favorable reports concerning the intravenous use of sodium amytal would indicate that it was very widely used in this manner. It is Woodbridge's

impression, however, that its intravenous use is rather restricted, but that it is a very popular and well established narcotic for administration by mouth and by rectum. The greatest enthusiasm is expressed over the elimination of the psychological strain on the patient incident to approaching the operating room and having the anesthetic administered.

J C McCann and J Fallon (New England J Med 204 358 (Feb 19) 1931) gave sodium amytal intravenously in 130 selected surgical cases. It induced only a basic hypnosis, and additional anesthetics were needed to eliminate reflexes and relax muscles. There were no discomforts with induction such as occur with inhalation or local anesthesia. Ether was always the supplementary anesthetic except for thyroid operations, for which nitrous oxide-oxygen was used. The amount of ether needed was less by 25 to 75 per cent than would have been required had ether alone been used. Amytal caused a transient fall of blood-pressure which, when necessary, was controlled by epinephrin. All patients convalesced with much less discomfort than usually follows operation. Nausea and vomiting occurred in only 21 of 130 patients. Patients slept about  $4\frac{1}{2}$  hours after operation and were lethargic for the next 24 hours. They remembered little of the experience on the day of operation. Sensibility to pain was reduced, so that they needed little morphine after operation. Pulmonary edema was the only serious complication. It occurred twice in the presence of advanced cardiac disease, once when there was a past history of lung abscess, and once when there was no such history. Three of the 4 patients died from pneumonia. Urinary retention occurred a little more often than with ether alone. Restless-

ness developed as consciousness returned, but morphine controlled it satisfactorily.

E B Ferguson (New England J Med 204 363 (Feb 19) 1931) believes that the oral administration of sodium amytal is superior to the intravenous routes because it eliminates the period of greatest apprehension just prior to operation. It is also simpler, less time consuming, and less hazardous. In a small percentage of cases the effect is uncertain, because the effect of the same dose on each individual varies, and in an endeavor to be safe, an insufficient amount may be administered. In such cases morphine sulphate,  $\frac{1}{6}$  grain (0.01 Gm), may be administered in the operating room.

The postanesthetic effect of sedative doses, has been satisfactory. Nausea and vomiting have been very much diminished and in most cases absent altogether.

Woodbridge (*loc cit*) claims that pulmonary edema and death occurred mainly in the case of large doses, or of elderly patients with marked weakness or vascular sclerosis. It appears that the incidence of pulmonary edema following intravenous administration has been less than 1 per cent; that the mortality has been 0.3 and 0.6 per cent.

**NEMBUTAL** (Sodium Ethyl-I-Methyl-Butyl Barbiturate) — Woodbridge (*loc cit*) states that nembutal is similar to sodium amytal, of which it is an isomer. It is effective in smaller doses. Those who use it preoperatively prefer it because of its shorter action and relative freedom from late restlessness and excitement. Its use seems to be spreading, encroaching on the field of sodium amytal.

**PERNOCTON**.—This is a 10 per cent aqueous solution of the sodium

salt of the secondary butyl-B-bromallyl barbituric acid R Brown, H Moloy and M Laird (Am J Obst and Gynec. 22 225 (Aug) 1931) report its use as an analgesic at the Sloane Hospital for Women in New York in 133 obstetric cases and as an adjuvant anesthetic in 20 gynecologic cases. They believe the use of pernocton in labor is a distinct advance in obstetric analgesia, producing analgesia and amnesia. The average dose was 4.4 cc (70.4 minims) intravenously. The first injection was given to 100 patients in the first stage and to 33 in the second. The effect was favorable in 130 patients, there being complete relief of pain from  $\frac{1}{2}$  to 4 hours. There was no tendency to prolong labor but the occasional tendency to cause (in 24 patients) varying degrees of restlessness, requiring restraint in some cases, is the only unhappy finding.

The average dose in gynecologic cases was 6 cc ( $1\frac{1}{2}$  drams) intravenously, preceded usually by morphine. The immediate effect was unconsciousness but there was restlessness in one-half of the patients, which, therefore, required nitrous oxide inhalation. There was a marked decrease in the use of sedatives for pain after operation.

This drug appears to be popular in Germany but to have made little headway in this country. R H Fitch, R M Waters and A L Tatum (Am. J. Surg. 9:110 (July) 1930) recommend this and nembutal preoperatively as the 2 most rapidly acting derivatives of barbituric acid. K C McCarthy (Anesth. and Analg. 9:231 (Sept-Oct) 1930) finds it twice as powerful as sodium amytal when used intravenously, whereas J S. Lundy (Anesth. and Analg. 9:210 (Sept-Oct.) 1930; Minnesota Med. 13:679 (Oct.) 1930) reports it to be less powerful.

**PHENOBARBITAL.**—“*Matin sleep*” anesthesia is the name G. F. Chandler (Am J Obst and Gynec. 21:285 (Feb) 1931) has given to routine administration of 10 grams (0.65 Gm) of phenobarbital to adult patients between the hours of 9 and 12 the night preceding an operation and followed with gas-ether at operation in the morning. He summarizes the advantages of “*matin sleep*” thus: It eliminates the mental hazard. The use of only about one-third the usual amount of ether is necessary. Little morphine is required. Patients are quiescent for 2 days following the operation.

**AVERTIN** (Tribromomethanol) — Avertin was first introduced by German chemists in 1926, and later used by English anesthetists. During the past 2 years, avertin has been available in this country for purposes of anesthesia. It is tribromomethyl alcohol, kept stable by the presence of amylene hydrate. Each cubic centimeter (16 minims) of the liquid represents 1 Gm (15 grains) of avertin. It is administered by rectal injection, and the solution is made by adding distilled water at 40° C. (104° F) and shaking thoroughly. It is recommended that a 2½ to 3 per cent solution be used and the temperature kept between 38° and 40° C (100.4° and 104° F). When heated above 40° C. (104° F), it decomposes into dibromacetaldehyde and hydrobromic acid, which are highly irritating to the bowel. Tests for purity of the solution should be made immediately before injection by observing its reaction with Congo red. This precaution should not be omitted. Avertin is detoxicated by the liver, and eliminated by the kidneys. It is excreted at a comparatively slow rate; experiments show that between 50 and 70 per cent. is excreted in the urine.

and recovered as bromine in the first 24 hours

**Dosage.**—The dosage is regulated by body weight E B Ferguson (*loc cit*) gives 80 to 100 mg ( $1\frac{1}{4}$  to  $1\frac{1}{2}$  grains) per kilogram ( $2\frac{1}{5}$  pounds) body weight in  $2\frac{1}{2}$  per cent. solution The author claims that this provides a good basal anesthetic upon which deeper narcosis may be imposed by nitrous oxide and oxygen The author also states that unlike oil-ether colonic administration, the patient experiences no abdominal cramps or discomfort of any kind

During the past year W E Dandy (J A M A 96 1860 (May 30) 1931) has almost exclusively used avertin anesthesia for all major operations on the brain and spinal cord The author claims a safe dose of avertin for a normal healthy individual is from 90 to 95 mg ( $1\frac{1}{3}$  to  $1\frac{3}{8}$  grains) per kilogram ( $2\frac{1}{5}$  pounds) of body weight Rarely is a greater dose given and never more than 100 mg ( $1\frac{1}{2}$  grains) per kilogram Smaller doses are given when the general condition of the patient is less than normal For a well nourished individual, a dose as low as 50 or 60 mg ( $\frac{5}{6}$  to 1 grain) per kilogram may be adequate

According to Horstenegg (Schmerz 111 210, 1930), in Spitzzy's Clinic, avertin narcosis is employed only for children because the child's heart, lungs, liver and kidneys are fairly resistant The author reviews 115 narcoses in 109 children 6 months of age and older A 2 per cent solution of avertin was used The dose was 0.125 Gm (2 grains) per kilogram ( $2\frac{1}{5}$  pounds) body weight The author's observations indicate that avertin narcosis is entirely safe for children

E B Ferguson (*loc cit*) states that

in obese individuals it is wiser not to give the full amount of the drug that their weight calls for The author thinks that large doses are responsible for bowel and rectal irritation

**Indications**—W E Dandy (*loc cit*) states that avertin is perfectly safe if used with good judgment The dangers have been fully enumerated by a number of German surgeons (J Schwalbe (Deutsche med Wchnschr 53 2064 (Dec 2) 1927, 54 558 (Apr 6) 1928) who pioneered in its use But there can be no doubt that their mortality rate has been due to overdosage, which in turn has been due to the effort to induce anesthesia with avertin unsupported This is neither necessary nor advisable The susceptibility of different individuals to the effect of avertin varies too much to produce maximum anesthesia safely by avertin alone And, once given, the avertin is rapidly absorbed and beyond control To obtain the best results with safety, an average dose should be given and any remaining deficit in the anesthesia may be overcome by supplementing a local anesthetic, ether by inhalation or nitrous oxide Dandy believes, for these reasons, that it is preferable to look upon avertin as a basal anesthetic He has used it during the past year in over 250 major cranial operations of every type, without anesthetic mortality, no instance of post-operative pneumonia, and no deleterious effect, either immediate or remote

According to E B Ferguson (*loc cit*), in a series of general surgical operations avertin has been used with satisfaction as a basal anesthetic. In the abdominal operations, the operators have observed greater muscular relaxation than is possible with nitrous oxide alone or in combination with sodium

amytal, although the tendency to blow the intestines into the wound is not entirely obviated. In operations outside the abdominal cavity it seems to offer advantages, especially in orthopedic cases, because it produces good muscular relaxation for approximately 2 hours and a long period of quiet following operation.

H. J. Stander (Am J Obst and Gynec 22 219 (Aug) 1931) has employed avertin anesthesia in a number of **gynecological operations** and in **cardiac disease** necessitating operative interruption of pregnancy, with good effect. In women the administration of avertin (tribromethyl alcohol) in a dosage amounting to 100 mg ( $1\frac{1}{2}$  grains) per kilogram ( $2\frac{1}{5}$  pounds) of body weight, produces no change in the blood chemistry. Avertin anesthesia seems especially indicated, therefore, in patients in whom general inhalation anesthesia is contraindicated and who show no disturbance in hepatic or renal function.

**Contraindications.**—According to E. Melzner (Deutsche med Wchnschr 56 1736 (Oct 10) 1930), the contraindications to the use of avertin are parenchymatous diseases of the kidneys and all affections that lead to renal diseases, such as sepsis. Hepatic diseases also constitute a contraindication to the administration of avertin because it is excreted from the body through the bladder combined with glycuronic acid and its detoxication depends chiefly on the liver. Avertin should be avoided also in all interventions that cause an acute diminution of the respiratory volume or the pulmonary surface, such as phrenic exeresis and extensive thoracoplastics.

Dandy (*loc cit*) writes that he has found no conditions that contraindicate

avertin when a general anesthetic of fairly long duration is needed. Pulmonary lesions, chronic nephritis and hypertension are apparently not contraindications. He has given this anesthetic to patients up to the eightieth year when ether would have been hazardous. In young children (under age of 8 or 10) Dandy has used avertin more sparingly, still preferring ether because the induction period is short and the total amount of ether required is small.

**Physiological Action.**—Dandy (*loc cit*) states that the only effect produced that might be considered adverse is a drop of blood-pressure, coming on within the first half-hour and usually within 15 minutes. In hypertensive cases a drop of 100 mg of mercury has been observed. In spite of this, the patient's color is good and breathing full and easy, and within a short time the blood-pressure has spontaneously returned to the previous normal level and remains so during the remainder of the operation. The drop in blood-pressure is, therefore, of no practical concern. It is, in fact, no longer considered necessary to support the blood-pressure with epinephrin, which may or may not be effective.

M. Bruger, W. Bourne and N. B. Dreyer (Am J Surg 9:82 (July) 1930) made a study of effects of this anesthetic and report that, like sodium amytal, avertin affects but slightly liver function (dye retention test) and blood hydrogen-ion content. The carbon dioxide combining power increases in the first half-hour and then falls off, but not severely. Avertin causes a sharp rise in blood sugar, which returns to normal in 6 to 24 hours. Renal function, as measured by volume of urinary output and the concentration and total

volume of urea, is depressed to a degree equal to that produced by ether and considerably greater than that produced by sodium amytal. Phosphoric acid excretion is increased. The rectal temperature of dogs falls slightly more than it does with sodium amytal.

C S White and J Kreiselman (Surg Gynec Obst. 51 361 (Sept) 1930) examined the blood of numerous patients 24 hours after avertin anesthesia and found the white blood count increased by over 600 per cmm, a slight negligible decrease in hemoglobin percentage and red-cell count, no change in clotting time or in blood sugar, an increase of 4.5 mg of nonprotein nitrogen per 100 cc, and a decrease in chlorides.

The soporific effect of avertin, according to Melzner (*loc cit*), depends upon resorption. If the avertin reaches the blood in sufficient concentration from the very beginning, sleep ensues under all circumstances. With rectal administration, the concentration in the blood depends upon resorption through the intestinal mucous membrane and the amount administered.

**Antidote for Avertin.**—According to F G Spiedal (Am J Surg 9 73 (July) 1930) and R M Waters and C W Muehlberger (Arch Surg 21 887 (Dec) 1930), the best antidote for avertin appears to be caffeine given intravenously.

**Mortality.**—Waters and Muehlberger (*loc cit*) report 2 deaths, 1 from obstruction of the airway 3 hours after operation in a child 18 months, the other 10½ hours after operation in a patient with brain tumor. Another death reported by H H MacWilliam, (Brit M J 1 1141 (June 22) 1929) was that of a healthy young adult undergoing inguinal herniorrhaphy. In re-

porting the case, the author concluded that "he failed to eliminate the drug."

In Germany, W Anschutz, K Specht and Fr Tieman ("Die Avertin-narkose in der Chirurgie," p 80, Springer, Berlin, 1930) collected reports of 103 deaths and considered most of them due to improper use of the drug.

D von Klimbo (Policlínico (sez chir) 36 474 (Sept 15) 1929) quotes Killian as having collected particulars of 3496 operations under avertin anesthesia. Among them were 16 deaths attributable to the drug itself. In 4 of these fatal cases there was necrosis of the bowel. Other surgeons have reported thousands of cases without a death.

**ANESTHESIA, SPINAL.—INDICATIONS AND ADVANTAGES.**—According to W W. Babcock (Cyclopedia of Med 1 519), spinal anesthesia is applicable to patients of all ages, from the newborn to those of advanced life. It can often be used when ether is inadmissible, as in patients with acute pulmonary or serious cardiovascular disease.

The author emphasizes its chief value in operations on the *lower abdomen* and *pelvis* and particularly is the procedure valuable in *acute peritoneal infections*, as from the *appendix*, a *perforated peptic* or *intestinal ulcer* or *strangulated hernia*.

B Rapoport (New England J Med 204 1254 (June 11) 1931) also states that there is no contraindication of any kind to spinal anesthesia except a moribund condition of the patient. Patients with hypertension and hypertensive heart disease furnish the largest number of bad reactions. Extreme age presents no contraindication.



L F Sise (New York State J Med 29 1182 (Oct 1) 1929) states one of the most striking advantages of spinal anesthesia is the intense muscular relaxation, the stomach and small bowel are in a state of tonic contraction, respiration is shallow and quiet. This combination of extreme relaxation, contracted intestines, and quiet respiration makes exposure and manipulation easy. Strong retraction and large tight packs become unnecessary. The relaxation afforded in abdominal operations, is not obtainable in any other way. Deep ether anesthesia cannot equal it—and deep ether anesthesia induces toxic disturbances.

As outlined by Babcock (*loc cit*), one of the greatest advantages of spinal anesthesia is that it *prevents* to a remarkable degree the production of *shock* by operative measures carried out under its influence (though it accentuates pre-existing shock). Its great rapidity of action—surgical analgesia being almost invariably induced within 2 minutes—is often of advantage.

Secondary nausea or vomiting should not occur as a result of spinal anesthesia, and the patient should have less post-operative pain, less headache, less backache, and less general discomfort than if he had received ether. The suffusion of the skin, drenching sweats, and heat radiation of ether are absent. Albuminuria does not occur. Preexisting toxemia is not accentuated. In no other way can as great an anesthesia be produced by the introduction of so little toxic substance into the body.

**CONTRAINDICATIONS.**—Quoting W W. Babcock (*loc cit.*), spinal anesthesia is not a measure to be recommended without skilled and continuous supervision. In from 2 to 5 per cent. of the patients coming to operation,

the injection, unless used with great care, involves unusual risk to the patient. For many of these cases, local anesthesia should be substituted on account of its greater safety. Once given, the spinal anesthetic cannot be withdrawn.

The determining factor in the success and safety of spinal, as with other anesthetics, is the user rather than the drug employed. If spinal anesthesia is dangerous, it is because it is used carelessly and without recourse to the necessary safeguards and antidotal measures. If it is ineffective, it is because the technic has not been acquired. If there are frequent postoperative headaches or other unpleasant symptoms, it is because something has been done that should not have been done. If a writer reports fatalities, he also reports his personal incompetence. Whereas in aneurism, threatened decompensation in valvular heart disease, in the excessive vascular tension of eclampsia, in nephritis, and in advanced arteriosclerosis, the vasorelaxation induced by spinal anesthesia may be of protective value, still the procedure should be used with care and in diminished dosage or else its use should be avoided. In conditions of marked hypotension, *e.g.*, in severe shock and where great depression or exhaustion of the spinal centers exists, spinal anesthesia is contraindicated. Patients nearly pulseless from traumatic shock should not, as a rule, be subjected to spinal anesthesia until reaction has occurred. The low blood-pressure induced also favors cardiac arrest in certain forms of myocardial disease, as well as in thoracotomy and other operations causing sudden changes in intrathoracic tension.

Patients with far advanced peritonitis, marked abdominal distention, and



cyanotic extremities, especially when of the middle aged, obese type, patients in collapse from traumatic ileus, patients with advanced septic disease of the biliary system and associated marked myocardial weakness, those with coronary occlusion, and patients greatly depressed and toxic, or with mechanical limitation of respiratory space, as from large serous or purulent effusions or massive intrathoracic growths, are not good subjects for spinal anesthesia. Local anesthesia should be substituted in most of the cases if the patient is *in extremis* or nearly moribund.

Obese patients with a short, thick chest and limited breathing apparatus are less suited for the method than subjects with ample breathing space. Aged and debilitated patients should receive relatively small doses of the anesthetic.

Greatly depressed subjects, who may be carried through an operation with local anesthesia or a few whiffs of ether, should not be given the spinal injection. Its use is rarely warranted for a minor operation.

Should spinal anesthesia be administered to a person with marked circulatory hypotension, preparations for an instant intravenous introduction of epinephrinized saline solution should be made before the operation.

Spinal anesthesia should not be employed by those who have not developed a trustworthy aseptic technic or have not carefully mastered the physiology of the method, including an understanding of the dosage and mode of diffusion of the drug. Neither should the procedure be used if the patient cannot be properly watched for 1 hour after the injection, or if the operator is unprepared to meet emergencies.

#### DRUGS AND DOSAGE USED.

—Although various drugs have been

tried at different times, *novocaine* is the drug mainly used at present, either in prepared solutions or the crystals.

B Rapoport (*loc cit*), commenting on 968 cases of spinal anesthesia, where novocaine crystals have been employed, concludes that the maximum dose should not exceed 200 mg (3 grains) of novocaine. The author states that large doses are tolerated by many patients but such doses are, however, too frequently hazardous; 200 mg (3 grains), then, is the maximum, 150 mg ( $2\frac{1}{3}$  grains) the average, and 100 mg ( $1\frac{1}{2}$  grains) the minimum dose.

W W Babcock (Med Times and Long Island M J 59 315 (Sept) 1931) states that the dosage to be used varies with the drug and with the size of the spinal canal. The patient's weight really has nothing to do with it, as a local and not general effect is produced. Obviously, because a patient is fat and weighs 200 or 300 pounds does not mean that the spinal canal is any larger and that the nerve roots require more anesthesia than in the case of a patient who weighs only 130 pounds. Indeed, if a patient is very heavy, especially if he be fat, it is dangerous to give a large dose and a small dose is preferable because such patients do not stand hypotension well. The mass of fat around the heart, chest and abdomen interferes with breathing. A thin, active patient will withstand a larger dose of the drug, other conditions being equal.

In infants aged 1 year, one-quarter the adult dose can be given with relative safety, infants stand spinal anesthesia rather well. Patients of advanced age do not stand it as well as younger patients. At 6 years, one-half the adult dose may be given—a child aged 6 years weighing 40 pounds (18 kilograms) may be given half as much as

that given a man weighing 200 pounds (90 kilograms) As the patient advances beyond middle life the amount of the drug is cut down

**UNTOWARD REACTIONS AND COMPLICATIONS.**—According to B. Rapoport (*loc cit*), the most dangerous reactions and fatalities have occurred within the first 5 to 10 minutes after the injection of the solution. *Respiratory paralysis* is usually the cause of early death, since invariably patients who died soon after induction of the anesthesia have complained of difficulty in respiration. The later reactions are mainly caused by depression of the circulation, which, in turn, is due to vasomotor dilatation. These reactions are always preceded by a marked drop in blood-pressure, weak pulse, pallor, perspiration and weakness. A complaint of difficulty in respiration should be of immediate concern to the anesthetist. Severe reactions are ushered in by persistent vomiting, profuse perspiration, extreme pallor, marked restlessness, weak and thready pulse, and zero blood-pressure.

Rapoport states that **caffeine** and **adrenalin** are the most effective stimulants when untoward effects are encountered. *Difficulty in respiration* is an alarming symptom, especially when accompanied by *cyanosis*. It should be treated with **carbon dioxide** and **oxygen**, and **artificial respiration**.

H. Koster and M. Weintrob (Am. J. Surg. 8 1165 (June) 1930), after an extensive examination of the literature on spinal anesthesia, as well as upon 6000 cases in the author's practice, state that *headache* is the most troublesome and most frequent sequel of spinal anesthesia. It occurs in about 20 per cent of all cases. The cause is still unknown. It has been found to occur least

frequently in patients who have been given plenty of fluids before operation. There are 2 types. One is made worse by raising the head, and is believed to be associated with diminution of cerebrospinal fluid. This form is relieved by the administration of **saline infusion**. In the other type there are symptoms of meningitis. In meningismus the cerebrospinal fluid is increased and relief is to be sought through the use of **diuretics**, **cathartics** and **hypertonic saline solution** given by the mouth or intravenously. A patient in the author's service was immediately relieved by the intravenous injection of **magnesium sulphate**.

*Incontinence of feces* is a very rare sequel and has always been transient. *Retention of urine* occurs occasionally. One patient had to be catheterized for 18 months. The writers found that this complication is much more frequent after inhalation narcosis than after spinal anesthesia. It occurs usually after operations involving the pelvis or perineum.

*Oculomotor paralysis* may begin immediately after the spinal puncture or not until the second week afterwards. It usually lasts 7 to 10 days. One patient did not recover for 2 months. *Abducens paralysis* is usually ushered in by a preliminary photophobia. There may be a functional *optic neuritis* with complete, though temporary, *blindness*. It must be remembered that eye complications similar to these may occur after lumbar puncture where no injection was made. *Meningismus* occurred in 10 per cent of the author's cases. The symptoms were headache, stiffness of the neck, inequality or sluggishness of the pupils, and photophobia. The symptoms lasted for 2 or 3 days and then subsided spontaneously. Nine

cases of *purulent meningitis* have been reported among hundreds of patients who have been given spinal anesthesia. Sepsis, except at the site of puncture, is no contraindication to the use of spinal injections. Damage to the spinal cord or to the nerve roots may result in areas of *anesthesia* or *paresthesia*, in *ulcers*, in *pain* along the course of nerves, in transient *anal* or *vesical incontinence*, or in *trophoneurotic changes* leading to atrophy of muscle groups.

In a series of 1010 operations done under spinal anesthesia by the writers there were 3 cases of *pneumonia*, 11 of *bronchitis*, 4 of dry *pleurisy*, and 1 of *massive collapse of the lung*.

J B Deaver and J C. Eckel (New England J Med. 203:760 (Oct 16) 1930) using spinocaine and apothosin in 2302 cases, found *headache* in 5 per cent of the cases, while Jackson (Am Surg 91 256 200 (Feb) 1930) in 1000, found *headache* in 15 per cent, and transient *paresthesias* in 04 per cent. Two needles were broken in the back.

#### PHYSIOLOGICAL ACTION.—

**Effect on Spinal Fluid.**—The spinal fluids of 31 cases were examined by A. H. Iason, M. Lederer, and M. Steiner (Surg Gynec. Obst 51.76 (July 1) 1930) 18 hours after spinal anesthesia. Of 14 cases, 11 showed a definite pleocytosis, 10 cases being of the lymphocytic variety, 1 of the polymorphonuclear variety. Seventeen cases were not considered because of the presence of red blood cells in the spinal fluid. In 20 of the 31 cases examined there was an increase in the spinal fluid sugar averaging 37.3 per cent. There was no change in the albumin, globulin or colloidal gold curves. Thirteen of the 31 cases developed mild postanesthesia sequelæ. There was no correla-

tion between the occurrence of post-anesthesia sequelæ and the changes observed in the spinal fluid. The technic of spinal anesthesia caused in certain instances a mild meningeal reaction but apparently does not produce serious organic changes, as reflected in the change of the composition of the cerebrospinal fluid.

**Effect on Spinal Cord and Its Membranes.**—L. Davis, H. Haven, J. H. Givens and J. Emmett (J A M. A. 97 1781 (Dec 12) 1931), in an experimental study conclude that the spinal anesthetic solutions in common use today are hemolytic as well as myelolytic and would seem to act on the myelin of the nerve fibers as they do on the lipoids of the red blood cell membrane, causing its dissolution.

After the injection of the spinal anesthetics in most prevalent use today into the spinal dural sacs of dogs, the following changes have been observed:

- 1 A varying degree of inflammatory reaction in the leptomeninges.

- 2 Passive changes in the ganglion cells of the gray matter of the cord similar to those seen in retrograde or so-called Wallerian degeneration.

- 3 Swelling and fragmentation of the axis cylinders.

- 4 Signs of degenerative changes in the fiber tracts of the cord.

The fact that the last 3 of these changes were not pronounced in the cords of animals which were allowed to live 90 days, speaks against their permanent nature. This is also suggested by the incomplete picture of degeneration of the ganglion cells and the absence of Marchi evidence of degeneration in the cervical and dorsal segments. However, the inflammatory changes in the leptomeninges were so constantly present that they cannot be overlooked.

**MORTALITY.**—According to H Koster and M Weintrob (Am J Surg 9.234 (Aug) 1930), there have been numerous fatalities following operations performed under spinal anesthesia. Some of these were probably due to the type of anesthetic employed, but a great many others apparently had no relation at all to the anesthesia. Statistics regarding deaths from spinal anesthesia will vary with the experience of surgeons employing this form of anesthesia, those from clinics in which subarachnoid block is used routinely, showing a much lower death rate than those from hospitals where spinal anesthesia is used only occasionally. Death usually occurs soon after the introduction of the anesthetic into the subarachnoid space, whereas death due to inhalation anesthesia may not occur until a considerable time after the completion of the operation. The danger of respiratory failure from the action of the drug upon the medulla consequent on its upward diffusion is negligible. The explanation of deaths following spinal anesthesia requires greater care in the study of the phenomena attending such fatalities and through autopsies. The authors review a series of fatalities cited by Rygh and Bessesen.

In the discussion of the value of spinal anesthesia before the Society of Surgery in Paris in 1923 and 1924, 20,267 cases were reviewed in which this type of anesthesia was used with 10 deaths. The authors analyze these fatal cases, 4 fatal cases which they reported in 1928, and several others.

In the authors' total number of almost 6000 general surgical cases there were only 6 deaths on the operating table. In all of the fatal cases the operation was performed under spinal anesthesia.

B Rapoport (*loc cit*) believes that every fatality from spinal anesthesia could be avoided, and may be attributed to a mistake on the part of the anesthetist. Every fatality that came to his attention, whether from this series or from reports of other men, could be traced to some definite error. Either the dose was too large, the drug not of the proper kind, the technic faulty, or the patient not fit for spinal anesthesia. On the other hand, some deaths occurring on the table or soon after the patient is put to bed may be due to hemorrhage, surgical shock, large thymus, or many other causes, and yet the blame for the fatality may be laid to the spinal anesthesia. In this series of 1875 cases there were 2 deaths which were caused directly by the spinal anesthesia.

## ANIMAL EXTRACTS. ADRENAL ORGANOOTHERAPY.

—Desiccated adrenal gland substance has been prescribed for many years as a therapeutic agent and is said to be of value in numerous conditions. The majority of the pharmaceutical houses have preparations on the market and literature abounds with claims of benefit following its use.

R G Hoskins and F. H. Sleeper (Endocrinology 14:109 (Mar-Apr.) 1930) examined a series of 130 cases in a diagnostic therapeutic study on the patients, more than half of which showed signs of functional deviation which indicated endocrine deficiency. The conditions noted were reduction of body temperature, fall in the blood-pressure, low basal metabolic rate, secondary anemia and reduction of bodily vigor, which findings suggested adrenal deficiency. The administration of adrenal substance alone, or in combination with other remedies was tried. A small

series of 9 patients were selected in which satisfactory test conditions were obtainable, and the adrenal substance was administered by mouth in dosages varying from 18 to 90 grains (1 1 to 6 Gm) daily, and for periods of 54 to 108 days. In 8 cases the adrenal substance was used alone, and in 1 it was given with thyroid. The subjects were all males and the ages ranged from 23 to 40 years. The results of the study were essentially negative throughout. No physical or mental changes were noted and these investigators conclude that desiccated adrenal substance given in large doses by mouth is of no significant therapeutic value. This is similar to findings of other observers.

The injection of adrenalin in cases of liver disease, diabetes and several other pathological conditions, causes less of a rise in the blood sugar level than occurs in normal patients as proven by R. F. Loeb, E. B. Reeves and H. P. Glasier (J. Clin. Investigation 10:19 (Apr) 1931). Following adrenalin injections, the blood sugar curve is in no way characteristic of liver disease, nor does it appear to correspond closely to the type or degree of pathology present. Following the administration of adrenalin hypodermically, the lactic acid curves are frequently lower in the cases of liver disease, diabetes mellitus and other conditions than those found in normal individuals. Loeb and his colleagues are of the opinion that the small response of the blood sugar and lactic acid in hepatitis, and especially diabetes, is from an inhibition of the action of adrenalin in carbohydrate metabolism. The pressor effect of adrenalin appears similar in normal individuals and those suffering from diseases of the liver, except in cases with carcinoma of the pancreas in which obstruction of the bowels

has taken place, where the effect is diminished.

#### **Adrenal Cortical Hormone.—**

Among the brilliant advances credited to medical science in the past decade, none have been more noteworthy than that of the isolation of a cortical hormone from the adrenal gland for the treatment of **Addison's disease**. Several laboratories have attacked this problem and independently have achieved substantial results. Notable among the investigators are Swingle and Pfiffner, Hartman, Koehler, Rogoff and Stewart. In approaching the problem of Addison's disease from the standpoint of therapy, L. G. Rowntree, C. H. Greene, W. W. Swingle and J. J. Pfiffner (J. A. M. A. 96:231 (Jan 24) 1931) offer the following points of value; (1) the nature of the underlying disease and its therapeutic approach; (2) the natural course of the disease; (3) general care of patients; (4) the treatment of symptoms and complications, and (5) the results of specific organotherapy. In general treatment, these investigators prescribe sufficient *rest, relaxation, warmth* to the body, *freedom from work and worry, protection from stress and strain* of all kinds, both *mental and physical*, and an *adequate amount of food and fluid*. They stress the value of *dextrose solution*, 10 per cent concentration and sodium chloride 1 per cent given intravenously during the crises and terminal stages of the disease, since in the latter course of Addison's disease marked dehydration is the rule.

If the disease be due to tuberculosis or syphilis, appropriate *specific therapy* is indicated, but care should be taken in order that the treatment does not further destroy the suprarenal glands. In a report on the clinical study on 20 patients, L. G. Rowntree, C. H. Greene,

W W Swingle, Ball and J J Pfiffner (Tr A Am Physicians 123, 1931) described in detail the effect of the use of cortical hormone. Unfortunately, the supply of this preparation was inadequate and, therefore, not all of the patients were given sufficient specific treatment. The immediate results of treatment were excellent in 15 of the 20 cases. Five of the patients died, 3 at home and 2 while under treatment, and most of the deaths appeared due to inadequate treatments because of insufficient supply of the hormone. These observers state that only 1 patient died who received an adequate amount of the cortical substance. Patients *in extremis*, however, may be beyond aid, even with an adequate supply of the substance available.

The *beneficial effects* of the use of the hormone are proven by the following clinical findings: (1) Disappearance of anorexia, nausea, vomiting and pain; (2) development of appetite and return of digestive activities; (3) relief from fatigue and improvement in sleep; (4) return of strength and endurance; (5) increase in weight; (6) disappearance of pigmentation; (7) total change of mental attitude with access of hope and euphoria; (8) slight and secondary increase in blood-pressure; (9) resumption of normal functions and desire to work; (10) increased resistance of infection, drugs and surgical procedures. Laboratory findings of significance are, as stated by these investigators, (1) increase in basal metabolic rate; (2) nitrogen retention with gain in weight; (3) improved kidney function with consequent lessening of the retention in the blood of urea nitrogen and sulphate; (4) disappearance of creatinuria; (5) disappearance of achlorhydria, as noted in 1 case.

In addition to cortical hormone, it is wise to pay attention to the general care of the patient, including rest, quiet, diet and symptomatic treatment, (2) the prevention and alleviation of dehydration, (3) attention to the underlying disease and its complications.

These observers use single doses of from 1 to 20 c.c. (16 minims to 5 drams) of the cortical hormone without untoward effects in the majority of cases. The treatment, as a rule, consists of the administration of 40 to 60 c.c. (1½ to 2 ounces) over a period of 4 to 10 days, and it has been without untoward effect. In the more severe cases, the course of treatment has been about 3 days, and in less severe about 10 days.

At the expiration of the effective time, during which the cortical hormone substance has been working within the body, if the patients receive none further, they begin to lose weight with loss of appetite and vomiting. These clinicians prefer intravenous administration, since it has given good results with no irritation to the patient. When the condition is under control, however, intramuscular injections are desirable. There is a slight local irritation attendant upon the hypodermic medication. The maximal daily maintenance dosage is probably from 3 to 5 c.c. (48 to 80 minims) of the cortical hormone, which signifies that the condition of the patient will probably be maintained at a normal level with from 3 to 5 c.c. (48 to 80 minims) a day, or about 1 liter (quart) a year. The amount of hormone necessary is proportional, as with insulin in diabetes, to the amount supplied by the adrenal glands; many patients having but partial destruction of the glands may not require as large a quantity as others who have considerable



amounts of the gland destroyed One c c (16 minims) of the cortical hormone elaborated by Swingle and Pfiffner is equivalent to the active hormone from 30 Gm (1 ounce) of cortical substance

The summary of these investigators concerning the cortical hormone of Swingle and Pfiffner is that it is a specific remedy in the treatment of **Addison's disease** and a most potent preparation The effect on hunger, food ingestion, and weight increase and strength is striking It must be kept in mind, however, that the remedy is not invariably of value, and cases in which the disease was only moderately advanced showed no response to what Rowntree and his colleagues believe to be adequate amounts of the cortical hormone Usually, however, the immediate effects of the drug for use in the crisis of Addison's disease are just as striking as the effects of insulin in the acidosis and coma of diabetes Since Addison's disease is a chronic condition due to tuberculosis of the adrenal glands, as a rule, substitution treatment constitutes only one of the problems to be solved, and the tuberculosis itself has to be handled On this account, Rowntree and his associates are careful to state that only the immediate results of the treatments with cortical hormone in Addison's disease have been observed at the present time A long series of cases over several years will have to be studied before the final appraisal of this important preparation can be made

**PITUITARY GLAND.—Preparations.**—S Janssen (Klin Wchnschr 9 1853 (Oct 4) 1930) has prepared a potent and stable product by dehydrating the fresh chopped *anterior lobe* of the pituitary in water-free acetone After removal of the acetone, the pow-

dered gland is kept over phosphopentoxide which preserves the potency both qualitatively and quantitatively The powder of 50 glands serves as a standard preparation and he observed the effect of this preparation on the size of the glands of female rats He found his preparation inactive when administered orally as was the case with all commercial preparations up to 0.6 c c (10 minims) dosage

**Physiological Action.**—V Rondelli (Policlinico (sez prat) 36 1665 (Nov 18) 1929) brings out the statement that hypophyseal secretion administered subcutaneously in appropriate doses exerts a peristaltic action on the colon, not associated with secondary effects of hypotension and dehydration, by a direct action on the muscle fibers and not on the mucosa These are nonhabit forming or accumulative effects

J B Ross and R L Stehle (J. Pharmacol and Exper Therapy 38 451 (Apr) 1930) report that the immediate cessation of urinary secretion is not the result of a ureteral spasm chiefly They believe it is not even an important factor.

J B Ross, N B Dreyer and R L Stehle (J of Pharmacol and Exper Therapy 38 461 (Apr) 1930) have determined the coronary flow and peripheral output simultaneously before and after the administration of pituitary extract The coronary spasm is believed by them to be at least one important factor which causes a fall in blood-pressure. The possible complications due to a constriction of the pulmonary vessels and of a direct action upon the heart muscle are discussed by the authors.

A Loeser (Klin Wchnschr 9 1855 (Oct 4) 1930) points out that the changes resulting from pregnancy involve not only the genitalia but the en-



ture incretory system, changes having been observed in the thyroid, hypophysis and ovaries. Although during pregnancy ovulation is normally suspended, Zondek succeeded in initiating it in pregnant mice by means of a hypophyseal extract.

Loeser also administered the hormonal extract either intramuscularly or subcutaneously. One ovary was removed as a control. The ovary that had been exposed to the action of the anterior pituitary hormone showed besides the corpora lutea graviditatis, also large follicles at the point of rupture and extensive hemorrhages. The follicles were filled with blood and from the wall of the follicles, luteinization had set in. This investigator also demonstrated by serial section that these changes were not pathologic, but that there was a regular ovulation with expulsion of the egg.

With experimental male rats C. R. Moore and L. T. Samuels (Am. J. Physiol. 96: 278 (Feb.) 1931) found a diet deficient in the antineuritic fraction of vitamin B or insufficient diets containing an excess of vitamin B resulted in normal seminiferous tubules in active spermatogenesis, but the prostate and seminal vesicles were castrate in type. Daily injections of either testis hormone or anterior hypophysis hormone from pregnancy urine into animals with castrate accessories resulted in the castrate condition being replaced by a normal state within 10 days. It is believed the injection of hypophysis hormone stimulates the intact testes to secrete their hormone which, in turn, acts on the accessories.

B. Zondek (Zentralbl. Gynak. 55: 1 (Jan. 3) 1931) has been one of the foremost investigators on the problem of the association of the *hypophysis and the placenta*. He found regarding this

association that (1) in pregnant women the blood, as well as the urine, contains excessive amounts of the hormone of the ripening of the follicles as well as the hormone affecting luteinization, (2) the human placenta contains hormones, however, only in comparatively small quantities—from 2 to 3 per cent of the quantity found in the blood and urine, (3) the anterior lobe of the hypophysis of the pregnant woman contains either no hormones at all or only extremely small quantities.

F. Gruter and P. Stricker (Klin. Wchnschr. 8: 2322 (Dec. 10) 1929) described experiments on domestic animals which prove that the *anterior pituitary gland* secretes a hormone which stimulates the mammary gland. The incomplete mammary gland was not affected by this hormone. Animals before puberty were also unaffected by it. If a production of corpora lutea through the administration of the anterior pituitary extract could be obtained, then the second hormone in the extract would stimulate lactation. They found this hypophyseal extract functioned with exceeding rapidity. Experimental work with extracts of liver, lung, posterior lobe of the pituitary, or placenta were disappointing as far as the secretion of milk was concerned.

W. Falta and F. Hogler (Klin. Wchnschr. 9: 1807 (Sept. 27) 1930) have investigated the action of the hormone of the *anterior lobe* of the pituitary gland. Body heat as represented by the basal metabolic rate is markedly diminished by the administration of an extract of the gland. Hormonal preparations they found only influence carbohydrate metabolism when insulin is present. In some instances an increased sensitivity to insulin was developed. Two cases of *infantilism* were stimu-

lated to growth by the extract, but there was no success in 2 cases of eunuchoidism. The authors believe the varied actions of anterior pituitary extract are the result of several rather than one distinct hormone.

**Therapeutics.**—The use of *posterior lobe* extract as a substitute for epinephrin is described by P. Wermer (Klin Wchnschr 9 779 (Apr 26) 1930) in which he applied it successfully in **local anesthesia**. It was found suitable for **laryngological operations**, in **tonsillectomy** and in **dentistry**. For surgical interventions the dose is from 5 to 10 Vogtlin units of hypophyseal extract to 250 c c (8½ ounces) of a solution of procaine hydrochloride, for **tonsillectomies** from 1 to 3 units for 30 c c (1 ounce) of procaine solution and in **dentistry** ½ unit for 2 c c (32 minims) of a 2 per cent solution. With the use of a hypophyseal extract there is an absence of the palpitation, tachycardia and intestinal complications.

The use of the *posterior lobe* extract as a **nasal spray** in doses of 0.5 c c (8 minims) once, twice or three times a day to produce one or more physiological bowel movements has been described by A. Sophian (J Missouri M A. 27 384 (Aug) 1930). About 1 to 7 hours after the spray a natural movement occurred without cramps. Soon the dosage was reduced and this therapy was advised in many types of patients other than those suffering from an atonic constipation.

**Functional uterine hemorrhage** is often encountered at puberty, during the adolescent period or during the reproductive period. Curettage is indicated for diagnosis and therapeutic purpose but recurrences are common.

The ovaries of these patients show an absence of corpora lutea and a persist-

ence of the unruptured Graafian follicle, denoting an excess of the follicle stimulus with an entire absence of the pro-gestation phase normally contributed by the corpus luteum.

E. Novak and G. B. Hurd (Am J Obst and Gynec 22 501 (Oct) 1931) report the treatment of 51 cases of this type, by an anterior pituitary luteinizing principle derived from the urine of pregnant women. In 44 of these cases the treatment was successful in checking the bleeding. This substance, containing chiefly prolactin B, produces luteinization in the ovary, and the secretion of the lutein cells is progesterin, the element lacking in functional hemorrhage.

In 14 of the 51 cases the bleeding ceased after a single injection and in 12 after 2 injections. Novak believes that this immediate effect is exerted upon the still unknown bleeding factor which is the immediate cause of the bleeding in functional hemorrhage and which is influenced by far smaller dosage than would be required to produce histologic changes in the ovary.

**OVARIAN ORGANO-THER-APY.**—**Preparations.**—A new era was ushered in when Doisy, of St. Louis, announced at the thirteenth International Physiological Congress, held in Boston in 1929, the isolation of an ovarian hormone in crystalline form. The Council on Pharmacy and Chemistry of the American Medical Association adopted the name "*theelin*" selected by Doisy, as the nonproprietary designation to be used in New and Non-official Remedies for the ovarian hormone made by the process of E. A. Doisy. S. A. Thayer, Louis Levin and J. M. Curtis (Proc Soc Exper. Biol. and Med 28 88 (Oct) 1930) then reported the discovery of a second estrogenic substance in the urine of pregnant

women It is a triatomic alcohol for which the name *theelol* has been proposed Injections of very small quantities cause opening of the vagina of sexually immature rats and mice, while injections into castrated adult rats produce the cornification of vaginal cells, characteristic of estrus

E A Doisy and S A Thayer (J Biol Chem 91 641 (May) 1931) note that *theelol* is 6 or 7 times as active as theelin in immature female rats, whereas it is approximately one-half as active in adult castrated rats With castrated rats assays of several preparations of theelol have given 1500 rat units per milligram, of theelin 3000 rat units According to Doisy and Thayer, 2 different substances exist in the extracts of the urine of pregnant women which are effective in producing changes in the genitalia of female rats

The work of E A Doisy and his co-workers C D Veler and S. Thayer (Editorial J A M A 94 341 (Feb 1) 1930) gives added impetus to the work on the *female sex hormone* They have been successful in isolating the female sex hormone in pure crystalline form The foundation of their work was based upon the presence of the hormone in the urine of pregnant women and the potency of it was such that the refined product in oil was equivalent to 2,000,000 Doisy-Allen units or over 8,000,000 mouse units

**Administration and Dose.**—In discussing the peroral *versus* subcutaneous administration of female sex hormone W Schoeller, M Dohrn and W. Hohlweg (Am J M Sc 182 326 (Sept) 1931) review the history of the progress along this field of research The stability of the follicular hormone makes it possible to administer it hypodermically, by mouth, by rectum

and by vagina The authors carried out extensive animal experiments with the peroral form of administration They found that the necessary peroral dose of *progynon* dragées showed a practically constant relationship to the subcutaneous dose of 4 to 1 These animal experiments would appear to justify the peroral administration of the hormone in human therapy

**Physiological Action.**—Experimentally treating guinea-pigs with extracts from various glands of internal secretion, N Candela (Arch di ostet e ginec 37 97 (Mar) 1930) found that *follicular extract* caused an increased development of the genital tract, maturation of the ovarian follicles, and prolongation and intensification of oestrus *Mammary extract* was found to cause atrophy of the ovaries and genital tract. *Follicular extract* caused slightly more marked hypertrophy of the thyroid and breast than lutein and mammary extract. Both follicular and mammary extract caused marked hypertrophy of the suprarenals and hypophysis, whereas *extract of corpus luteum* produced atrophy of the hypophysis and moderate hypertrophy of the suprarenals.

The recent work on follicular and corpus luteum hormones is summarized briefly by E. Allen (J. A. M A 97. 1189 (Oct. 24, 1931) The outstanding animal reaction to *follicular hormone*, "*theelin*," is growth of the accessory genital tissues. A considerable series of quantitative tests have been made of the follicular hormone content of human genital tissues. Fluid aspirated from follicles of human ovaries at operation was injected, and solid ovarian tissues were implanted in subcutaneous pockets in ovariectomized rats. The full estrous growth of the vaginal wall was used as an indicator of positive reactions. Posi-

tive tests were obtained from fresh follicular fluid removed from the ovaries at operation, 0.37 c.c. (6 minims) being the least amount effective. The tissue walls of large follicles returned positive results when single pieces weighing as little as 0.18 and 0.22 Gm. (3 and 3½ grains) were implanted. Allen emphasizes the variation in physiologic response among different laboratory animals when injected with theelin.

In recent corpora lutea, corresponding to ova recovered from the tubes, the smallest amount to return positive reactions were 0.07 Gm. (1¼ grains) an unusually high yield for living tissues.

Specific reactions attributed to the *corpus luteum hormone* are summarized as follows:

(1) Hisaw has induced resorption of the symphysis pubis of the pocket-gopher and relaxation of the pelvic ligaments of the guinea-pig such as normally occurs in these animals at parturition, by the "one-two action" of follicular (theelin) and corpus luteum ("relaxin") hormones.

(2) Corner and Willard Allen and Hisaw, independently, have produced progestational endometrium in rabbits and premenstrual endometrium in monkeys. Since in all cases the action of theelin must precede that of this corpus luteum hormone, "*progestin*," the latter is obviously complementary to theelin.

(3) Hisaw has induced the mucous transformation of the superficial layers of the vaginal epithelium of rodents, which is characteristic during pregnancy.

(4) Ripening of the follicles and the onset of estrus have been delayed by injections of corpus luteum extracts. Similar results have been obtained, however, with extracts of testis and also extracts of other ovarian tissues; there-

fore, it still seems doubtful whether this last effect can be considered a specific corpus luteum reaction.

(5) The contraction stimulus of pituitary solution on the uterus has been inhibited by corpus luteum extracts.

Slower progress in the exploration of sources and the production of biologically standardized purified extracts of corpora lutea must be expected.

**Therapeutics.**—C. C. Norris and C. A. Behney (Surg. Gynec. Obst. 49: 642 (Nov.) 1929) report 31 cases in which they followed the technic of Blair-Bell in *transplantation of ovarian tissue* when the removal of the original was imperative. They divided the tissue to be transplanted into many small sections, hoping for better vascularization. The grafts were introduced into the rectus muscle with strict asepsis and hemostasis. Of the 31 cases operated, the authors report 25 being traced. Six in which the uterus was conserved menstruated regularly, of 19 subjected to hysterectomy, 42.1 per cent were free of menopausal symptoms, 21 per cent showed mild symptoms, and only 10.5 per cent were severe.

**PLACENTAL ORGANOTHERAPY.**—A. D. Campbell and J. B. Collip (Brit. Med. Jour. 2: 1081 (Dec. 27) 1930) have isolated an ovarian-like (85 per cent alcohol soluble) and an anterior pituitary-like fraction (85 per cent alcohol precipitate) of placental extract.

The observations reported by these investigators deal in the main with the possible therapeutic value of the ovarian-like fraction. In all, 123 normal patients with clinically deranged ovarian function were treated and observed for periods varying from 3 to 9 months. A dose corresponding to 75 Gm. (2½ ounces) of placenta daily,

given in divided doses in water or orange juice, before meals, has been used in the majority of the cases. Some patients do not tolerate the extract well. In any case in which untoward symptoms, such as nausea or vertigo, were observed the dose was temporarily reduced until tolerance was acquired.

There was no effect on impregnation or gestation. Four patients became pregnant while under treatment for ovarian dysfunction. There was no effect on libido. The dosage used in cases of *dyssmenorrhea* was as a rule the equivalent of 25 Gm ( $6\frac{1}{4}$  drams) of placenta administered daily for approximately 17 days beginning with the cessation of the menstrual period. During the week preceding menstruation the dose was raised to 75 Gm ( $2\frac{1}{2}$  ounces) daily.

The second principle or anterior pituitary-like substance of placenta was employed in *metrorrhagia* with encouraging results. The extract contained 10 rat units per c.c. administered subcutaneously. It should be borne in mind, however, that diagnostic uterine curettage should always precede treatment for *metrorrhagia*.

#### PARATHYROID GLAND.—

*Physiological Action.*—Studying the effect of parathyroid extract on the diffusibility of calcium in human beings, Cantarowa (Arch Int Med 44 834 (Dec) 1929) found that it does not affect either the diffusible or the non-diffusible fraction of serum calcium. The most marked increase in nondiffusible calcium occurred in patients in whom the factor was originally low, as in those with bronchial asthma. That the diffusible and nondiffusible values may vary independently is evidenced by the fact that at times the 2 increased simultaneously, while at other times an

increase in one was accompanied by a decrease in the other. That the level of diffusible calcium is not entirely dependent on the total serum calcium is shown in cases in which the former factor increased coincidentally with a diminution in the latter. The same point is illustrated strikingly in cases in which the reverse condition prevailed, *viz.*, a decrease in diffusible calcium coincidentally with an increase in the serum calcium. It appears that the parathyroid hormone in some cases showing a normal calcium distribution causes a preliminary increase in the ratio of diffusible to non-diffusible calcium, followed by a more marked and prolonged decrease in this ratio. In other instances, particularly with a low nondiffusible fraction, the ratio decreases steadily over the 12 hour period. Variations in the ratio do not bear a constant relation to the total serum calcium.

A most interesting discussion of the results of a study of the progressive changes in blood chemistry during an overdosage of parathyroid hormone has been made by J. B. Collip (Canad M A J 24:646 (May) 1931). He reports the gradual increase in the blood calcium to 20 mgm per 100 c.c. of blood. It remains at this height and then falls a few milligrams in the terminal stages. The inorganic phosphorus of the serum is practically unaffected until the blood serum calcium has reached a level of 15 mgm. per 100 c.c. From this point on it rises rapidly until death ensues. At the same time the kidney function is diminished and the nonprotein nitrogen rises well over 100 mgm per 100 c.c. of blood. Acidosis of a marked degree also occurs. Dogs were maintained by Collip in a state of mild hypocalcemia over a period of weeks by small daily doses of

the hormone without ill effects, but there was a marked loss of skeletal calcium through excessive excretion in the urine of calcium salts

**SPLEEN.**—P Tremonti (Riforma med 46 1383 (Sept 1) 1930) experimented with the venous blood from the spleen and found that when injected into the jugular vein, it caused a reduction in the blood-pressure and a hepatic enlargement. The injection of acetylcholin had a similar effect and for this reason the author concluded that acetylcholin may be the active principle of the spleen.

The injection of pig spleen prepared in an isotonic solution of sodium chloride in cases of **protracted convalescence** and **malnutrition**, especially in cases of suspected **tuberculosis**, has given most gratifying temporary results to F L Soler (Revista de especialid 4 1097 (Oct) 1929). The dose was 3 c c (48 minims) for adults twice weekly for 10 injections.

#### **ANOREXIA. — TREATMENT.**

—R S Allison and R P Davies have recently discussed the treatment of functional anorexia in a paper based on a study of 20 such cases at Ruthin Castle (Lancet 1 902 (Apr 25) 1931). Although the condition is usually mild and temporary, following some psychic shock or worry, it may become extremely severe, progressing into anorexia nervosa which is occasionally fatal. A preliminary study to rule out organic disease and to estimate the degree of anorexia is essential, according to the writers. The approximate number of calories taken daily is an index of the severity of the disease. Treatment consists of increasing caloric intake while decreasing energy output. Foods of little bulk but of high caloric value and of attractive nature should be used. To

be sure that ample food is being fed, the writers consider that the basal requirements should be calculated and a considerable excess fed. Bitter tonics such as **gentian**, **strychnine**, and **dilute hydrochloric acid** are often of value. The use of insulin did not result favorably in the cases cited. Some writers have suggested the use of thyroid extract in extreme malnutrition based on the finding of low metabolic rates in starvation. Allison and Davies, however, do not recommend its use. **Gastric lavage** is valuable in cases of chronic gastritis and ptosis, the best time for its use being late afternoon, according to the authors, since many of these patients with ptosis have faulty gastric emptying, and withdrawing the residue at this hour improves the appetite for dinner.

**Periodic fasting** has also been used by the writers, a fast day being enforced about every 3 days. It has been found that immediately following this almost complete fast, rapid weight gain usually occurs. A diet of **water and orange juice** is allowed during the fasting period, with about 2000 calories being fed on the other days. **Bed rest** is necessary during the first part of such treatment.

**ANTIPOLIOMYELITIS SERUM.**—An immune horse serum elaborated for use against **poliomyelitis** has been described by M Neustaedter (J A M A 96 933 (Mar 21) 1931). An ideal preparation has not as yet been obtained, since this author reports violent reactions with high fever from 104° to 106° F. (40° to 41.1° C) and sometimes convulsions and coma following the intraspinal injection of the preparation. The use of the serum intramuscularly and by intravenous routes



appears to avoid any of the untoward effects occasioned by intraspinal injections. The safest method to forestall an anaphylactic reaction, according to Neustaedter, is to give the patient a  $\frac{1}{4}$  grain (16 mg) of *morphine* and  $\frac{1}{100}$  grain (0.6 mg) of *atropine sulphate*, and wait several minutes before injecting subcutaneously a few minims of the antipoliomyelitis serum. If at the end of a 10-minute period there is no reaction, Neustaedter advises that it is safe to proceed with the intramuscular or intravenous injection of the serum. From 20 to 30 c.c. ( $\frac{2}{3}$  to 1 ounce) of the unconcentrated serum may be given to adults every 24 hours or on alternate days, according to the severity of the case. The dosage for children has to be calculated according to age and also the advance of the disease. Injections may be given daily until the temperature drops to normal or after this period, if clinical indications are present, until 10 injections in all have been given. A Herxheimer reaction defines the limit of safety. When the disease is particularly severe or advanced, Neustaedter advises that the intramuscular and intravenous routes be used simultaneously, giving the concentrated serum in 5 c.c. (80 minim) doses. By the intramuscular route, a Herxheimer reaction usually appears after the third dose, and the serum seems to be better tolerated intravenously.

Neustaedter reports good effect from the use of antipoliomyelitis horse serum in more than 60 cases of fully developed paralytic cases of **poliomyelitis**. The chronic cases with elevation of temperature over a long period of time, should likewise be given serum, although the results are apt to be less striking than when the acute stage is present. The serum can be standardized and obtained

in sufficient quantities at the present time.

**ANURIA.** See URINARY RETENTION.

**APPENDICITIS.—INCIDENCE.**—In the period from 1920 to 1925 the incidence of appendicitis increased from 11 to 14.4 per 100,000 population. In the United States, about 20,000 persons die from the condition each year. Appendicitis occurs with equal frequency in males and females.

L. W. Tasche and J. P. Spano (Ann Surg 93:899 (Apr) 1931) have analyzed 700 consecutive appendectomies. Of the acute cases reviewed by the authors, 60.9 per cent. occurred in males, whereas of the chronic or interval cases, 61.4 per cent. occurred in females. In 75 per cent the condition appeared during the second or third decade of life. The average age of the patients was 21.9 years. Appendicitis is most common in the summer months, possibly because of the increased prevalence of gastrointestinal disorders in the summer. In 58 per cent. of the cases reviewed there was a history of recent infection. The most common preceding conditions were colds, sore throat and tonsillitis. Recent or simultaneous infections were more frequent in children than in adults. More than half of the patients had had previous attacks of appendicitis, and many of them were referred during an interval between attacks.

The cases were classified clinically as mild, moderate, severe, and very severe. Pathologically, they were grouped in the following 4 classes: (1) those with no evidence of active inflammation; (2) those of recurrent appendicitis in which previous infection was evidenced by perivascular collections of lymphocytes



in the serosa; (3) those of acute suppurative appendicitis, and (4) those of "obliterated appendix"

The most satisfactory classification was found to be the surgical-pathological. According to this classification, the cases were divided into the following 5 groups.

1 Appendicitis without suppuration

(a) Chronic appendicitis. This group included all cases with a definite history of appendicitis and many which should be classified as cases of acute or sub-acute subsiding appendicitis because tenderness was present over McBurney's point. In 339 interval cases there was 1 death, a mortality of 0.3 per cent. The patient who died was an obese woman whose appendix was located under the liver and whose cecum had not descended normally. Her death resulted from paralytic ileus which was attributed to the prolonged exploration necessary at the time of operation. (b) Acute appendicitis. There were 361 cases in this group with a mortality of 6.4 per cent.

2 Acute suppurative appendicitis: The 72 cases in this group included all cases of suppuration in which there was no peritoneal involvement or abscess formation. The mortality was 1.4 per cent.

3 Acute appendicitis with local peritonitis: In this group there were 156 cases with a mortality of 2.5 per cent.

4 Acute appendicitis with abscess: This group included 112 cases with a mortality of 9.7 per cent.

5 Acute appendicitis with diffuse peritonitis. In 21 cases in this group there were 8 deaths, a mortality of 38 per cent.

**DIAGNOSIS.**—According to D. P. D. Wilkie (Brit. M. J. 1:253 (Feb. 14) 1931), pathological changes and clinical

symptoms of appendicitis should be qualified in such a way that the subject will not be shrouded in difficulties and uncertainties, which make for hesitation and delay in diagnosis. In support of this, he recognizes 2 primary acute diseases of the appendix: (1) acute inflammation of its wall—appendicitis, and (2) acute obstruction of its lumen—a closed-loop intestinal obstruction.

**Appendicitis.**—Inflammation of the wall of the appendix is of common occurrence and may be the sequel to a blood-borne infection—as when it follows a tonsillitis—or to an intestinal catarrh. It is characterized by a turgid swelling of the wall of the appendix, frequently some ulceration of its lining mucosa, and, in some cases, by a plastic and occasionally suppurative local peritonitis. Clinically, its onset is, relatively speaking, a gradual one, characterized by nausea, pain, and constitutional disturbances in the shape of fever, accelerated pulse rate, dirty tongue, and usually constipation, but occasionally diarrhea. It is seldom a fatal disease unless complicated by an obstructive factor, by the sudden perforation of an ulcer due to a concretion, by a secondary intestinal obstruction, which is rare, or by an ill-timed operation.

**Acute Appendicular Obstruction.**—This is a very fatal form of intestinal obstruction, because it is of the closed-loop variety which tends to early gangrene. If it would but be realized that a sudden and complete obstruction of the lumen of an appendix, containing fecal matter, will, from the pressure of decomposing content, inevitably lead to tension gangrene within from 6 to 24 hours, and that gangrene will be followed by perforation, with the escape of foul fecal content into the free and unprepared peritoneal cavity, the recogni-

tion of the onset of such an obstruction would be regarded as one of the most important and responsible duties of a medical practitioner

The author cites a case history giving a typical clinical picture of this type of disease

Wilkie (*loc cit*) feels that acute appendicular obstruction is responsible for the greater portion of the present mortality in appendicitis, and that the majority of the patients now operated on early are of the class that do not contribute to the mortality

In cases in which peritonitis has developed, J B Deaver (Surg Gynec Obst 51 529 (Oct) 1930) has found auscultation of the abdomen a very valuable means of detecting the lesion He states that the stormy, the turbulant, and the silent belly are significant of stages of peritonitis, *i e*, they indicate whether it is circumscribing, circumscribed, diffusing, or diffused. In the early stages of peritoneal irritation, very delicate palpation will often reveal the presence of serous fluid It is important to determine the position of the appendix As a rule, the appendix is located at the site of the most marked tenderness and rigidity A deep pelvic position will require deep pressure to elicit tenderness and often lead to a mistaken diagnosis of diverticulitis of the sigmoid

**MORTALITY.**—According to J O Bower (J A M A 96 1461 (May 2) 1931), the mortality in the United States from acute appendicitis in the period from 1913 to 1923 was 22.3 per cent.; in Philadelphia it was 18 per cent. H A. Royster (Pennsylvania Med. J. 34 376 (Mar) 1931) estimates that in the year 1926, 17,335 persons died of appendicitis; 12,655 of these were given laxatives and 11,680 of the latter probably died from the effects of laxatives.

The author emphasizes that appendicitis is a surgical disease from the very beginning, and that the surgeon must not cease urging early operation The chief causes of the increase in mortality are delay of operation and the administration of cathartics early in the condition Reduction of the mortality depends upon the prevention of gangrene and perforation with consequent peritonitis Morrison says "There should be no percentage of deaths from appendicitis if every case commencing with acute pain and developing tenderness and rigidity of the abdomen and quickening of the pulse were operated on within 12 hours"

J B Deaver (*loc cit*) stated that the crux of the problem is diagnosis If the diagnosis is properly made, it means operation He stated that the operative mortality in acute appendicitis is high because the time for operation is not well chosen or because, if opportunely timed, the operation was incomplete because of the surgeon's poor judgment or his lack of experience in the treatment of appendicitis or both

**TREATMENT.—When to Operate.**—J. B Deaver (*loc cit.*) does not believe that acute appendicitis always necessitates an immediate emergency operation He emphasizes that surgical judgment is required to decide when to operate and when not to operate, and that the decision not to operate often requires greater deliberation Chill, abatement of the pain, and a drop in the temperature are 3 signals for immediate operation .

The time at which the operation should be done after *peritonitis* has developed depends upon the type of the peritonitis and the patient's condition. In circumscribed peritonitis with abscess, immediate operation with proper technic is safe unless there are forbid-

ding systemic or other conditions, which in these days of spinal anesthesia are not numerous

In *circumscribing peritonitis*, *i.e.*, cases in which the infection shows a tendency to become localized, Deaver employed anatomical and physiological rest, the **Fowler-Murphy-Ochsner treatment**. With few exceptions, the circumscribing peritonitis becomes circumscribed under this treatment and permits operation with little risk of death

In *diffused peritonitis*, postponement of operation is usually best. However, if the case is seen very early when the belly walls are still rigid, operation by an experienced surgeon promises most

**Appendectomy.**—A. H. Southam (Brit M J 1 258 (Feb 14) 1931) believes that the choice of *incision* in a case of acute appendicitis merits the serious consideration of every surgeon. The view taken by him is that in the McBurney muscle splitting incision the ilioinguinal nerve is liable to injury, and is sometimes followed by the appearance of a postoperative right inguinal hernia. The *paramedian incision* with outward displacement of the rectus muscle has the advantage that it can be safely extended to any length, this is undoubtedly the best incision for general exploration of the abdominal cavity in cases in which the diagnosis is in doubt and good access is required. In many cases, however, this incision will be found to be at some distance from the site of infection and will necessitate careful packing off of the small intestine to avoid the risk of soiling the general peritoneal cavity when an abscess is present. For these reasons there is much to be said in favor of a *lateral incision*

In typical cases of acute appendicitis

localized to the right iliac fossa and in young patients, Battle's *pararectal incision* with inward displacement of the rectus muscle is regarded as being highly satisfactory. This incision gives adequate exposure in such cases with the minimum disturbance of the inflamed parts, and as the nerves can be seen and readily avoided, it rarely leads to any subsequent weakness of the abdominal wall. No case of inguinal hernia following the use of Battle's incision during a number of years has so far been encountered.

**Drainage**—On the basis of 8 years' study, A. Muller (Wien k Wchnschr 43 1501 (Dec 4) 1930) discusses whether primary closure of the abdominal cavity or drainage gives the best results in appendectomy

Tabular reports indicate that if drainage is used there is a certain percentage of fatalities, whereas without drainage the mortality is zero. The author thinks that drainage is done too frequently and that primary closure of the peritoneum and of the subcutis should be done in all cases of acute appendicitis without severe complications. In gangrene or perforation of the appendix, the number of cases in which primary closure without drainage was done is still limited. However, the experiences in a small number of such cases speak for primary closure. The author asserts that drainage retards the healing process. He thinks that neither serous nor cloudy exudates necessitate a drainage tube, a strip of gauze or drainage thread. The gauze and the thread hinder the discharge of the secretion and cause congestion. It is also probable that the presence of the foreign body leads to excessive secretion.

When the pathological reports are negative as regards infection, J. B.

Deaver (*loc cit*) drains only in the presence of a green peritoneum and a subperitoneal exudate. In such cases drainage is necessary, since occasionally the exudate does not resolve but forms an abscess.

**POSTOPERATIVE COMPLICATIONS.**—P Chutro (Second Argentine Surgical Congress, 1930) divides the postoperative complications of appendicitis into 2 groups: (1) those of chronic, interval, and early acute appendicitis, and (2) those of suppurating, gangrenous and perforating types. While the operative technic and anesthesia may be responsible for many of the complications in the first group, the disease itself is responsible for those of the second group.

In case of suppurative, perforated, or gangrenous appendicitis, some form of complication occurs after operation in 60 per cent of the cases. The possible complications are peritonitis, phlegmon and suppuration of the abdominal wall, pylephlebitis, deep cellulitis, ileus, perforation of the intestine with fecal fistula, subphrenic abscess, epiploitis, secondary hemorrhage, embolism, phlebitis, respiratory complications, parotitis, enteritis, insufficiency of the liver, and acute dilatation of the stomach.

N H Brodersen (*Acta chir Scandinav* 66:101, 1930) reports a case of cecocolic invagination including 7 cm of the ileum following appendectomy, which he attributes to the invaginated stump. He believes that he may have taken too deep a suture in burying the stump, and that, as a consequence, the stump became polypous and was seized and carried upward by peristalsis.

**APPENDICITIS IN CHILDREN.—DIAGNOSIS.**—When acute appendicitis occurs in very young

patients, the *diagnosis* is frequently very difficult. A Hurlé Alvarez (*Nourrisson* 18:306 (Sept) 1930) described such an attack of acute appendicitis in a child 13 months of age and warned against the possibility of overlooking such an infection in patients of that age when gastroenteritis is so common. The important characteristics of appendicitis in very young patients are persistent vomiting, a high pulse rate in proportion to a moderate elevation of the temperature, and finally, a resistance of the abdominal muscles to deep pressure.

The fulminating and atypical character of appendicitis in 5 patients was reported by B. Portis (*S Clin North America* 10:359 (Apr) 1930). In this group, pain was a variable factor, usually beginning as a diffuse abdominal discomfort and later localizing in the right lower quadrant. All of them had some type of gastrointestinal disturbance, with loss of appetite, nausea or vomiting. Although there was pain and tenderness of the abdomen, muscular rigidity was not so marked. The leukocyte count, which the author had found to be increased to 15,000 to 20,000 in most patients with acute appendicitis, was only 4800 to 7200 in the 5 fulminating cases reported.

H Hornung (*Arch. f. Kinderh.* 91:299 (Oct 21) 1930) was able to make a diagnosis of chronic appendicitis in a child of 8 years of age by means of *x-ray* examination of the gastrointestinal tract. The child had had vague symptoms but the roentgenologic observation revealed a delayed filling of the appendix and a shadow defect suggesting a stenosis. Subsequent operation confirmed the diagnosis.

Many clinicians have doubted the value of the *x-ray* method of diagnosis.

ing chronic appendicitis but there have been several reports lately, giving encouraging results. For instance, H J Walton and S Weinstein (Am J Roentgenol 24 631 (Dec) 1930) made a diagnosis of chronic appendicitis in 152 instances in a group of 1000 consecutive gastrointestinal x-ray examinations in patients of all ages. Of this group 87.5 per cent had the diagnosis confirmed at operation. Likewise, R Finsterbusch and F. Gross (Arch f klin. Chr. 164 454 (Feb 17) 1931) have concluded that x-ray examination of the intestinal tract is a valuable aid to the clinical findings in patients with chronic appendicitis and in eliminating other false diagnoses. They followed a very detailed technic of roentgenography and based their conclusions on observations of 500 patients.

**MORTALITY.**—Although appendicitis is not common in children under 5 years of age, the mortality may be high in proportion to its incidence. This is apparently due to 2 factors: (1) the diagnosis is more difficult to make because often the classical signs are not present, and (2) the condition develops so rapidly that rupture and peritonitis occur within a short time. J R. Gerstley (M Clin North America 13 1175 (Mar) 1930) reviewed the age distribution and mortality of this disease. Although only 2 per cent of the patients with appendicitis are under 5 years of age, yet 4 per cent of the deaths from this infection occur in that age group. The author quotes the figures of Diess who found only 1 patient with the disease under 6 months of age and 1 between the ages of 6 months and a year out of a group of 466 admissions. There were 12 between the ages of 1 and 3 years (of a total of 1570 admissions), 11 from 3 to 5 (1090

admissions), and 40 from 5 to 10 (1593 admissions).

**ARSENIC.**—Potassium arsenite (Fowler's solution) has been used for many years in chronic myelocytic leukemia, but with the advent of x-ray therapy its use was fairly generally discarded. The procedure was revived, however, recently by C H Forkner and T F M Scott (J A M A 97 3 (July 4) 1931), who studied the effects of Fowler's solution in 10 cases of **chronic myelocytic leukemia**. Nine of the patients showed similar responses to treatment, with a reduction of the white blood cell count to normal or nearly normal, arrest of the progress of the anemia, reduction in the size of the spleen and liver, and general improvement in the patient's condition. These observers believe that the old empiric notions concerning Fowler's solution for chronic myelocytic leukemia can be supported by scientific data, since the drug seems to have a specific effect on the hematopoietic organs, producing a prompt reduction in the total number of the circulating white blood cells. The explanation of just how this change is brought about is not clear, however. In many ways, the results of treatment with Fowler's solution are similar to those produced by x-rays and by radium. The *dosage* required to produce a remission varies with the patient. The best results, as obtained by these observers, come from the rapid and relentless administration of the drug until the desired result is produced, or until beginning signs of intoxication occur. The drug should then be discontinued from 4 to 6 days and resumed in small daily doses. If completely withdrawn, the white cell count remains low for a period of 3 or 4 weeks, and then rapidly

rises The administration of the drug may be controlled by frequent studies of the blood slides and of the patient This is essential so that no harm may be done in the use of Fowler's solution for these cases

**ARSPHENAMINE.—POISONING.**—The use of a diet rich in carbohydrate for the purpose of preventing liver injury in cases requiring arsphenamine has been questioned by E B Craven (Bull Johns Hopkins Hosp 48 131 (Mar) 1931), who cites that Davis and Whipple, in 1919, originally demonstrated the influence of fasting and other diets on liver injury due to chloroform anesthesia These investigators found that a diet rich in carbohydrates produces a marked protective reaction against liver injury from chloroform, but on the other hand, fat-rich and protein-rich diets offered a maximum susceptibility to injury Craven points out that certain clinics are utilizing the practice of placing patients suffering from arsphenamine jaundice on a high carbohydrate diet

A number of experiments designed to test the protective action of the 3 principal dietary factors, *i e*, carbohydrate, fat and protein, against liver injury due to arsphenamine was arranged by Craven

Using a standard brand of arsphenamine, the acid arsphenamine was dissolved in sterile distilled water, so that each 10 cc ( $2\frac{1}{2}$  drams) of solution equalled 0.10 Gm ( $1\frac{1}{2}$  grains) of arsphenamine Later this was precipitated by the addition of 15 per cent sodium hydroxide, with enough excess hydroxide to redissolve the precipitate; a single drop of NaOH was then added and the solution filtered. Enough of this solution was made up fresh as re-

quired so that an entire series of animals received the same amount of the fresh drug Thirty dogs were used for this experiment, 10 were placed on a carbohydrate-rich diet, 10 on a fat diet and 10 on a protein-high diet The arsphenamine was given in exactly equal amounts based on the body weight of the animals The extent of liver injury, however, varied considerably The animals on the carbohydrate-rich diet showed extreme liver necrosis, with destruction of the entire lobule with the exception of a narrow zone around the portal spaces in 4 of the dogs, marked necrosis was observed in 5, while in 1 animal there was moderate necrosis Of the dogs on the fat-high diet, frank necrosis was present in only 1, and Craven is of the opinion that in this instance the injury was due to starvation The animals on the protein-high diet showed as follows: 4 were normal; 3 showed signs of slight central necrosis consisting of a narrow zone of necrotic cells about the central veins; and 3 showed a necrosis of one-tenth or less of the lobule, known as moderate necrosis

To test the theory that starvation was an important predisposing factor, an experiment using 4 dogs was performed Two of the animals were starved for 48 hours, but given as much water as desired, while the other 2 were fed a meat diet. Arsphenamine was then given in a dosage of 0.03 Gm ( $\frac{1}{2}$  grain) per kilo ( $2\frac{1}{5}$  pounds) body weight

The following day both of the starved animals were very ill; they vomited, became weak and listless and were jaundiced All 4 of the animals were sacrificed, the 2 starvation animals showed extreme liver necrosis, while the dogs given protein diet, showed no liver damage



Craven desired to ascertain why a patient receiving a series of injections of arsphenamine occasionally showed jaundice weeks or months after the receipt of the last injection. He states that it was possible that delayed jaundice might be due to a so-called carbohydrate debauch. The author kept a series of dogs on a meat-fat diet for several weeks and gave them weekly injections of arsphenamine. He then endeavored to give them a quantity of arsphenamine in weekly doses for a period of 3 weeks which would just fall short of producing jaundice. Following the 3 injections, the meat-fat diet was continued for a fourth week. Then Van den Bergh tests were made every other day for 4 weeks. This test was consistently negative on all the dogs. The diet was then switched to a high-carbohydrate with the hypothesis that this flooding of the animals with carbohydrates would add an unsupportable burden to the liver already subjected to 3 large doses of arsphenamine. Then the Van den Bergh tests were again performed every second day for a period of weeks, but none of the animals became jaundiced. At this time the dogs were sacrificed, together with a comparable series of control animals which had received identical quantities of arsphenamine, but had been kept exclusively on a meat-fat diet. At autopsy, no necrosis was found in any of the animals. The author believes that positive results in a similar repeated experiment are still possible.

To obtain this, however, the dogs should be loaded with a maximum quantity of arsphenamine that just falls short of producing jaundice.

Craven described the work of Voegtlin who, in 1925, showed that toxic effects of arsenoxides could be diminished in rats by the previous injection of

glutathione. Voegtlin maintained that the SH radical was the arsenic receptor and in such a combination the arsenic was rendered relatively nontoxic. Since cystine of the amino-acid also contains an SH radical, Voegtlin fed his experimental rats this acid and was in that way able to reduce the toxicity of trivalent arsenicals, although not to the same extent as he could accomplish with the use of glutathione.

Craven points out that his results are consistent with the facts proven by Voegtlin, in that the meat-fat diet presumably contains more cystine derivatives than carbohydrate diet. Cystine, therefore, added to the carbohydrate diet, should provide the otherwise absent sulphydril radicals and render the diet as efficacious in preventing liver necrosis as are meat and fat diets.

Craven experimented on 20 dogs, 8 of which were given cystine by stomach tube before the administration of arsphenamine. Two of the animals received arsphenamine in which had been dissolved 3 Gm (45 grains) of cystine, the remaining dogs were kept as controls and received no cystine. All of the 20 dogs were given the high carbohydrate diet for 4 days before the injection of arsphenamine. Three hours before the injection, 8 of the animals were given 3 Gm (45 grains) of cystine each by stomach tube, then a single large dose of arsphenamine, 0.03 Gm ( $\frac{1}{2}$  grain) per kilo ( $2\frac{1}{2}$  pounds), was injected in all 20 animals. In the case of 2 dogs, 3 Gm (45 grains) of cystine were dissolved in their portion of arsphenamine solution as mentioned above.

Autopsy revealed marked liver necrosis in all 20 animals, with advanced necrosis in several of them, and no differences were noted between the 2 series, those having received the cystine

showing just as marked necrosis as those having had none. Craven concludes that high fat and high protein diets provide the maximum protection against liver injury caused by arsphenamine, and of the 2, he recommends the high fat diet. High carbohydrates, on the other hand, produce a maximum susceptibility to liver damage caused by arsphenamine. Starvation also is important as a predisposing factor toward liver injury. Cystine added to the diet and given intravenously appears in no way to increase the protective action of carbohydrate diets.

J. W. Brittingham and T. Phinzy (J. A. M. A. 96:2021 (June 13) 1931) describe a case which developed hemorrhagic encephalitis following the injection of neoarsphenamine. This was a negro woman, aged 20, examined in the obstetric clinic at the University of Georgia Hospital, who showed a 4 plus Wassermann, and was referred to the syphilis division of the medical clinic for treatment. A preliminary course of bismuth salicylate, in doses of 0.13 Gm. (2 grains), at weekly intervals for 6 doses, were given and then neoarsphenamine was administered in a dosage of 0.45 Gm. (7 grains). She was given this drug in a dosage of 0.6 Gm. (10 grains) for 3 more weekly injections, and finally was delivered at term of a healthy appearing baby. She returned to the syphilis clinic and was given neoarsphenamine 0.6 Gm. (10 grains) which appeared well tolerated. A week later, a similar dose was given, which seemed to upset the patient. Following a rather difficult venipuncture, the patient complained of feeling weak and of a choking sensation, but got up and walked about the room. Two minutes later she suddenly screamed, complained of backache, and would have fallen to the floor

if not assisted. Because of the shock, epinephrine 1 c.c. (16 minims) in 1:1000 solution was given intramuscularly, and 15 minutes later the patient felt better, leaving the hospital an hour later.

Two days later, she was admitted to the hospital complaining of severe headaches, excitation and gradually increasing coma. The temperature was 102.2° F (39° C), pulse 130, respirations 44, and blood-pressure 160 systolic and 125 diastolic. There was clotted blood about the gingival margins. There were a few scattered petechiae on both breasts, and a small subcutaneous hemorrhage on the site of venipuncture were noted. Deep reflexes were all absent and the extremities were flaccid. The patient died the next day, and at autopsy the following significant findings were noted. A few petechiae were found in the myocardium; the visceral pleura as well as the epicardium showed petechiae; the liver weighed 1880 Gm. and the lobulations appeared irregular; the spleen weighed 230 Gm.; and the lymph nodules were barely visible. A large hemorrhage in the pia arachnoid of the medulla and upper part of the spinal cord was noted. On section, numerous minute petechiae were found in the cerebrum, cerebellum, pons and medulla. In the pons and lower part of the medulla, several of the hemorrhages were 4 mm in diameter. On microscopic examination, the hemorrhages were found and it was also noted that the erythrocytes were sickle-shaped. In sections of the brain, lungs, heart, liver, spleen, suprarenals, kidneys and pancreas the capillaries were filled with fat. Areas of focal necrosis were found in the pancreas.

These observers point out that in necropsy in all cases presenting this syn-

drome stains for fat should be performed at necropsy

**ARTHRITIS.**—In a splendid article on the Control of Arthritis by R B Osgood (New England J Med 204 55 (Jan 8) 1931) he refers to a recent house to house survey, organized by the Massachusetts State Department of Health and directed by Dr Herbert Lombard, in the cities of Brocton and Greenfield and their surrounding rural townships, which seems to show that nearly 10 per cent of the total population is suffering from some form of chronic disease. The number of people complaining of rheumatism and arthritis in these communities is twice as large as those complaining of heart disease, 8 times as large as those complaining of tuberculosis, and 20 times as large as those complaining of cancer. Careful investigations suggest that these percentages would hold throughout the whole State. In the Boston Survey of Chronic Diseases, 40 per cent of the arthritic cases had existed for over 5 years, largely outnumbering the long period disabilities of any of the other common chronic diseases. The frequent helplessness of these patients, their need of attendance, as well as their numbers, would seem to make them economically and socially the most important single group of patients with chronic disease.

To help consider, more intelligently, methods of control of this disease, it may be of value to state the conception which most careful workers now hold as to the 2 main types of chronic arthritis, their prodromal symptoms, and the broad general principles which underlie their sound treatment.

An International Committee for the Control of Rheumatism was organized, 3 years ago, and an American branch of

this committee, 2 years ago. It is made up of internists, surgeons and research workers who have been individually attempting to elucidate the problem of chronic arthritis. The American branch of the committee at the last meeting in Kansas City, in October, subscribed unanimously to the following statement as representing their concept of this group of diseases.

1. The disease, chronic arthritis, prevalent in all temperate zones, represents one of the most important, if not the most important, of existing social and industrial handicaps.

2. The Committee conceives of the disease as a generalized disease with joint manifestations. Certain prodromes may be recognized, and it is of vital importance that they be recognized.

3. It is the opinion of the Committee that at the present time no single infectious agent or any completely defined dietary deficiency or metabolic disturbance has been shown to be the sole cause of these disorders. The Committee inclines to the belief that any one of these factors, or certain combinations of these factors, under appropriate circumstances, may basically underlie the onset of the disease.

4. The Committee feels it of vital importance that the medical profession have its attention directed to the methods of treatment of proved value which are at present at its disposal. In spite of etiological uncertainties, the Committee feels that properly managed therapy, which takes into account both infectious and metabolic factors, has yielded results which encourage optimism and impose the obligation of further developing such methods.

5. In the light of the foregoing considerations, the Committee purposes to broadcast as widely as possible, both to the profession and to the public its concept of the nature of the types of arthritis included under the heading, chronic rheumatism, its belief as to the probable predisposing and exciting causes of the disease, and the knowledge which the Committee possesses or may acquire as to the most efficient methods of treatment.

Differentiation of chronic joint rheumatism or arthritis into at least 2 types is important for the general practitioner, for the details

CHART SHOWING DIFFERENCES IN INCIDENCE, ONSET, SIGNS AND SYMPTOMS, X-RAY APPEARANCES, AND MORBID HISTOLOGY IN THE 2 MAIN TYPES OF CHRONIC ARTHRITIS, DESIGNATED AS ATROPHIC ARTHRITIS AND HYPERTROPHIC ARTHRITIS

	Atrophic Arthritis	Hypertrophic Arthritis
Common synonymous terms employed in other classifications	Rheumatoid arthritis Proliferative or ankylosing arthritis Arthritis deformans Poker back spondylitis rhizomélisque, Strumpell-Marie type Still's disease (children)	Osteoarthritis Degenerative or nonankylosing arthritis Osteoarthritis of the spine, Von Bechterew's syndrome Malum coxae senilis
Age— Incidence— Body Type— Onset	From infancy to middle life  Somewhat more common in slender ptotic women and men Acute to insidious	From middle life to death  Somewhat more common in stocky well-nourished men and women Subacute to ignorance of presence
Symptoms and signs	General health usually not robust, fatigued easily Pain and disability often pronounced Joint swellings and muscle atrophy to be observed	General health usually less disturbed Pain and disability often slight Joint swellings and muscle atrophy less noticeable
Early x-ray appearances	No apparent cartilage or bone changes General increased density of soft parts Diminished density of bone atrophy—no "lipping"	Slight "lipping" of articular margins  No general increased density of soft parts Less diminished density of bone (unless long non-use).
Late	Narrowed articular space subluxations—ankylosis	Articular space irregular, hypertostoses. No ankylosis
Early Morbid histology	Early proliferation of synovial membrane—"pannus" Usually small round cell infiltration Epithelioid nests	Early fibrillation of articular cartilage No general proliferation of synovial membrane. No small round cell infiltration Chondroosseous hypertrophy of articular margins
Late	Late destructive and atrophic processes in cartilage and bone Fibrous, true, bone ankylosis	Late ebriation, deformation and hypertrophy of articular bone ends. Cyst-like cavities in cancellous bone near articular surface Joint mice common—no true bone ankylosis

of sound treatment may differ from the very different nature of both the early and late joint tissue changes in the 2 types

If the concept of the American Committee for the Control of Rheumatism is true, then rheumatism would seem likely to be prevented by cultivating the art of living in respect to the avoidance of over-fatigue, the establishment of good body mechanics, an appropriate dietary régime and elimination of known sources of toxic absorption. The general practitioner should be equipped to be the best instructor in this art of

living and the public should be educated and, if possible, induced to consult him often enough while they are in good health to check up on their needs and obtain this preventive instruction.

The *prodromal symptoms* of chronic arthritis are in order: (1) fatigue of body and mind, (2) elimination of fatigue poisons; (3) susceptibility as might be suggested by the asthenic or the sthenic body type, and (4) foci of ill-health. It is not to be understood that the importance of foci of infection are minimized but suggest the possi-

bility that they may be the *results* of ill-health as well as the *exciting cause* of ill-health. Under foci of ill-health are included elimination, food, vitamin and endocrine deficiency.

It has been estimated at the Massachusetts Hospital School that less than 5 per cent of more than 1500 orthopedic patients entering with large and apparently pathological tonsils, show any indication for tonsillectomy after a stay of several months, under the hygienic living conditions which this school provides.

The early joint signs and symptoms may be intermittent and fleeting but should never be ignored, for when they make themselves manifest the generalized disease has existed for a considerable period and permanent joint tissue damage is at least threatened and may have already taken place. If harmful influences are removed, certain joint tissues, especially the synovial membrane, possess the power not only of repair but also complete regeneration. Others, like the bone, may readily repair, but more rarely completely regenerate. Hyaline articular cartilage repairs with difficulty and, as far as is known, never completely regenerates after it has been damaged or destroyed.

The early joint of *atrophic arthritis* shows usually a little spindle-shaped swelling, often a little heat and tenderness to pressure. Perhaps the metacarpophalangeal and metacarpophalangeal joints of the hand are most likely to be affected first. The x-rays may show only the soft shadow of soft-part swelling, but usually the articular end of the bones will reveal lessened density of trabeculation and a narrowing of cortical shadow.

The early joint of *hypertrophic arthritis* may exhibit no signs and give rise

to few symptoms unless pushed to excessive use or accidentally traumatized. The x-rays may reveal the little chondroosseous spicules before they can be palpated, in even so superficial a joint as the knee. The patient may be entirely unaware of their existence. Even transitory stiffness on excessive use may be absent and a normal range of painless joint motion may be present.

The long existent joint of *atrophic arthritis* will usually present deformity, perhaps amounting to subluxation, a variable amount of swelling and heat, dependent upon the amount of local activity of the disease, a limitation of motion varying from half the normal range to complete ankylosis. The x-rays will reveal not only atrophic bones of lessened density, but with their articular ends altered in contour and diminished in size. These joints, unless the disease is inactive and repair processes have set in, almost never show any spiculation at the joint margins or any gross overgrowth of bone or calcium deposit.

The long existent joint of *hypertrophic arthritis* will present less gross deformity than the long existent atrophic joint. While its joint motion may be markedly limited, it will not be ankylosed. Unless it has been acutely lighted up, it will be puffy rather than swollen, tender usually only over the chondroosseous spicules or ridges, with no appreciable difference in surface temperature. The x-rays will reveal joint changes out of all proportion to the joint symptoms.

Unless the limb has been immobilized or disused, there will be no density of the shadow which it casts. At the joint margins and at the attachments of the tendons and ligaments, calcified overgrowths will be seen, and often in a joint with a large cavity, like the knee,

loose calcified bodies, the so-called joint mice are observed. The articular ends of the bones are often notched, with thin but dense articular surface eburnation and cyst-like cavities beneath the articular surface. A symmetrical destruction of the articular cartilage takes place, sometimes going on to complete absence of articular cartilage, but no bony ankylosis forms, as it does in the advanced joint of atrophic arthritis.

**TREATMENT AND CONTROL.**—If the present concept of the 2 types of arthritis is sound, a generalized disease must be combated, as well as its joint manifestations. A lookout must be kept for prodromal symptoms and signs which have been described and our house must be set in order at the earliest possible moment by seeing to it that:

1 Fatigue and excessive nerve outgo are eliminated

2 The body is well set up and is working on sound mechanical principles

3 The food fuel to run these machines is of the right sort and quantity and that the waste products of combustion and nutrition are regularly and completely carried off

4 Colonies of harmful bacteria, whether they represent cause or effect, be eliminated either by calling out the defense mechanisms of the body to gradually overcome them or by a direct surgical attack on their strongholds.

5 An examination is made of the various systems of the body—alimentary, circulatory, nervous, endocrine, etc., looking to the correction of any dysfunction of these systems by rest, by exercise, by training in body mechanisms, by physiotherapy, by drugs, by glandular substance, perhaps by surgery

When serious local joint symptoms present, the aim should be to arrest the disease by these same means, not by any single one of them, but by a combination of measures

In the *atrophic type* the individual joints tend to become flexed and con-

tracted. Prevention of deformity may be obtained by splints or other appliances. Muscles as well as bones tend to atrophy, voluntary exercise, then, in this type should be carried to the point of easy toleration

The affected joints of both types, but especially of the atrophic type have diminished blood supply. Inadequate fluid exchange, Millard Smith calls it. Pemberton and Pierce have demonstrated this loss of capillary control by direct observation of the capillaries and by thermometric control experiments; therefore, heat and massage are called for as well as exercise. And finally, when the disease is arrested, if the joint contractures still offer obstruction to the normal joint function, surgery may restore satisfactory degrees of usefulness and wage-earning capacity. The largest number of the arthritic cripples are of the atrophic type

Very little actual crippling results from the joint lesions of the *hypertrophic type* unless the hip joints become seriously involved. It is in this type that the fixation and protective appliances may be used with less care than in the atrophic type. Not only does such protection relieve the patient's discomfort, but it causes a subsidence of the signs of joint irritation, limited mobility, puffiness, tender chondro-osseous ridges, etc. It must not be too complete nor continuous and it must interfere as little as possible with the blood supply, which should be stimulated artificially by local applications of heat and light therapy. In both types diet and elimination are very important. Each case is a somewhat individual problem, but a diet rich in vitamins and poor in starchy and sweet carbohydrates is a safe working rule, and meat, red or white, is not harmful if the



amount is proportionate to the demands of activity

Milk is the most perfect of natural foods and ripe citrous fruits seem to do more good than harm. Overweight is to be avoided and the calories, in general, should be kept as low as possible to retain a normal weight.

In order to control chronic arthritis, Osgood (*loc cit*) considers that there must be an awakening of the healthy population to the need for control and an awakening of those sick with arthritis to the possibility of betterment. One large insurance company has just issued a Primer on Rheumatism prepared with the cooperation of the American Committee for the Control of Rheumatism. This should help the laity and may conceivably help some of the doctors as well.

At the recent congress at Liège it was decided that, at least for statistical purposes, a uniform nomenclature should be adopted for English, German and French writers. In English the 2 terms recommended were *rheumatoid arthritis* and *osteoarthritis*. Some of the terms which in the past have been used synonymously with rheumatoid arthritis are: atrophic arthritis, chronic infective arthritis and arthritis deformans. Hypertrophic arthritis is synonymous with osteoarthritis. The well-known pathologic studies of Nichols and Richardson, carried on some years ago, led them to use the pathologic descriptive term, "*proliferative arthritis*" corresponding to the clinical rheumatoid arthritis, and "*degenerative arthritis*" corresponding to the clinical osteoarthritis. The not infrequent presence of mixed forms of the disease in the same patient has given rise to considerable confusion. If the "*mixed forms*" is included as a third term in the classification, about 95 per

cent of the cases can be properly assigned

**PATHOLOGY.**—One hundred and forty-two stools from 40 patients with chronic arthritis were analyzed in a simple routine way by R. T. Moore and F. C. Hall (*Arch Int Med* 47:764 (May) 1931), the results being compared with those obtained on examination of 97 stools from 71 patients suffering from other diseases. No definite pathologic condition was found, except for the presence of starch in the stools from the arthritic group of patients: (a) Seventy-nine per cent of the stools showed an excess of starch, as compared with 26.8 per cent for the control group. (b) Iodine-staining organisms were found in the stools of 90 per cent of the patients, as compared to 22 per cent for the controls. (c) The fermentation test was positive in 82.5 per cent of the cases, as compared to 24 per cent for the controls.

Difficulty in the utilization of the starch, while occasionally found in a variety of conditions, is prone to occur in patients with chronic arthritis, and adds further evidence that diets low in starch are of use in this disease.

The *sedimentation rate* in cases of infectious arthritis is high (from 60 to 80 per cent) and does not usually return to normal, unless the cause is removed. This procedure does not differentiate the various types of secondary arthritis, such as tuberculous and gonorrheal arthritis or acute arthritis deformans. The high sedimentation rate is not due to the anemia that is usually present. This procedure is of no diagnostic value in arthritis but is of great help in the prognosis and an essential guide in treatment and convalescence according to A. Weiss (*Am. J. M. Sc.* 181:379 (Mar) 1931).

**ETIOLOGY.**—Many cases of arthritis cannot be explained on the basis of infection or toxemia

In discussing the *cerebral origin* of arthritis, Karl Rothschild (Ann Int. Med 4 1287 (Apr) 1931) states that the center for calcium metabolism, located in the subthalamic region of the brain, in the gray matter surrounding the third ventricle, may be affected in the diseases of the corpus striatum system (chronic encephalitis, Huntington's chorea, chronic chorea, paralysis agitans, Wilson's lenticular degeneration and Westphal's pseudosclerosis) If this center is affected, there will be changes in the quantitative or qualitative calcium metabolism, producing arthritis

The occurrence of similar signs in the above mentioned diseases of the brain and arthritis has caused observers to suspect a possible involvement of the nervous system and such changes may be considered as "aging" of phylogenetically old centers, not involving the pyramidal tracts

According to L G Rowntree, A. W. Adson and P S Hench (Ann Int Med 4. 447 (Nov) 1930), resection of the lumbar and the cervicothoracic sympathetic ganglia for the relief of so-called chronic infectious arthritis seems to further substantiate the claim that the nervous system plays an important part in the course of arthritis The results of 18 bilateral resections on 17 selected patients has been attended with gratifying relief of the neurocirculatory and trophic changes accompanying this disease

In order to determine the influence of incretory and constitutional factors on chronic polyarthritis, R Gantenberg (Deutsche med. Wchnschr 56. 1902 (Nov 7) 1930) investigated the clinical histories of 200 patients. In 14 of

these cases *endocrine disorders* existed and the chronic polyarthritis had developed at the same time However, it would not be entirely correct to speak of endocrine chronic polyarthritis in all these patients, because in some of the cases an infectious arthritis had gone before, and in others there existed tonsillar changes and other pharyngeal disorders, which made an infectious etiology appear probable In a few cases, however, no other cause but an endocrine disturbance could be detected The author emphasizes that the percentage of cases of chronic polyarthritis with endocrine etiology is small He also points out that chronic polyarthritis concurs frequently with tuberculosis The basal metabolism was likewise tested in order to determine the significance of incretory disturbances in the development of chronic polyarthritis However, it was found that the diagnostic value of these tests was slight Examination of the allergy of the skin likewise gave no practical results. In cases in which the pathogenesis involves endocrine factors, the therapy should employ **organ extracts**. **Paraffin packs** of the joints and **x-ray therapy** proved helpful in many cases.

### ARTHROPATHIES, TABETIC.

—Arthur Steindler (J. A. M. A 96: 250 (Jan 24) 1931) reports on 64 cases of arthropathy involving 99 joints, only 2 of which were definitely nontabetic. The author states that J K. Mitchell, in 1831, was the first to point to connection between cord lesions and certain joint diseases. Charcot, in 1868, connected tabes with the arthropathy which bears his name and Weir Mitchell, in 1875, added myelitis to the list. In 1892, Sokoloff reported 20 cases from the literature with 3 of his own cases

in which syringomyelia was the cause of arthropathies. Arthropathies are known to occur also in lesions of the cord following fracture of the spine.

From 4 to 10 per cent of tabetic patients acquire arthropathies and 25 per cent of cases with syringomyelia develop some form of neurogenic arthropathy. While these arthropathies are more common in the lower extremities in the tabetic patients, the upper extremities are more frequently affected in syringomyelia.

**PATHOGENESIS.**—A controversy as to the pathogenesis has long been carried on. Charcot considered the condition entirely of neurogenic origin. He felt that trophic and circulatory disturbances arising from the degeneration in the spinal cord were responsible for the joint changes. The mechanical traumatic theory was advanced, with the belief that external influences were necessary, in addition to the loss of nerve supply to the joint. (Eloesser has shown very convincingly that if the joint is protected by immobilization in a plaster cast, the removal of the nerve supply is not followed by the development of the arthropathy, whereas the joint so protected goes on to a typical arthropathy of the Charcot type as soon as the protecting immobilization is abandoned.) The controversy continues between those who see the loss of nerve supply as the sole and complete cause of the arthropathy, and those who explain the syndrome of tabetic arthropathy on the basis of analgesia, ataxia and injury due to overuse of a joint which has been robbed of its sensory nerve supply. The author reviews the experimental work and the pathology and histopathology.

The x-ray examination demonstrates all of the gross anatomic features. In

the weight-bearing joints there is marked erosion and as soon as the articular cartilage has been fragmented or destroyed, the grinding of bone upon bone results in a very rapid disintegration. This is especially apparent in the hips where the acetabula become tremendous excavations in which the eroded femora move about in an extraordinary manner. Often the head and neck of the femora are entirely fragmented. A great deal of new bone formation takes place in the form of callus and eburnation. Abnormal mobility is a very early finding in all of these joints and precedes the development of obvious x-ray evidence. In the advanced case the joint capsule has become tremendously thickened and enlarged and can best be described as a thick walled sac containing large amounts of bony debris (free bodies) and allowing of a high degree of abnormal mobility.

*Tabetic spondylitis* may show a relatively slight destruction of 2 adjacent vertebral bodies with or without abnormal mobility, and without much new bone formation, or it may go on to a formidable deformation with exuberant callus and tremendous fringe formation, with ossification of the long vertebral ligaments.

In the shoulder the advanced case may resemble the changes in the hip and there is a tendency to enormous joint effusions with many free bodies. In the elbow the essential findings are destruction of the bone ends and disappearance or disintegration of the joint space, with or without a great deal of callus, and usually with many free bodies. A valgus deformity is usually found.

**TREATMENT.**—In view of the impossibility of restoring the nerve supply, the best that can be hoped for is an

arrest of the progressive destruction. This depends upon **protecting the joint against the trauma** incident to its free use. Improvement in function is obtained by the use of **apparatus**.

**ARTHROPLASTY.**—In a very instructive article on the subject of arthroplasty, W. C. Campbell (*J. Bone and Joint Surg.* 13: 223 (Apr.) 1931) has made a careful study of the physiology on material obtained from biopsy in joints on which an arthroplasty had been performed. The evolution of the reconstructed joint is Nature's method of repair, and is exactly the same process that occurs by the motion or friction of raw osseous surfaces in ununited fractures and spontaneous arthroplasties after destructive lesions of joints. In a section of a knee on which arthroplasty had been performed and normal function obtained, the formation of 3 definite layers may be noted: (a) the superficial—fibrous tissue, (b) metaplastic cartilage, (c) cancellous bone.

**ASBESTOSIS.**—E. R. A. Merewether (*J. Indust. Hyg.* 12: 198 (May); 12: 239 (June) 1930) gives an account of an extensive and thorough study of the conditions in the English asbestos industry. No asbestos is mined in England, so this study refers only to workers engaged in manufacturing. Among the 374 workers subjected to a clinical examination, 11 suffered from a fibrosis which, presumably, came from exposure to dust in other trades, and they were, therefore, excluded from this group. Of the 363 remaining, 274 were engaged in the industry for more than 5 years. On this side of the water it is generally believed that a clinical examination is of little value in a study of this sort if unsupported by x-ray ex-

amination of the chest. The author is of the opinion that a diagnosis of pulmonary fibrosis can be quite confidently made on clinical examinations, except in very early cases. Emphasis is laid on a thin, high-pitched percussion note and a sense of resistance to the percussing finger; deficient expansion is common and actual retraction of the apices during inspiration. Indefinite auscultatory signs are recorded, such as weakening of the respiratory murmur, more especially at the bases. Unfortunately, there is no standard percussion note and no standard breath sound, so that alterations in these signs, unless unilateral, are not unequivocal. On the basis of the clinical examinations, 95, or 26.2 per cent, of the cases were classed as fibrotic, and 21, or 5.8 per cent, as pre-fibrotic. Radiological examinations were made of 133 cases, of which 39.1 per cent showed fibrosis and 16.5 per cent suggestive changes but not definitely diffuse fibrosis.

In addition to the clinical and radiological examinations of the workers, investigation of the dust count in the air of the workrooms was made. The instrument used was the Owens jet apparatus. This instrument may yield higher counts than the Greenberg "Impinger," which is the instrument commonly used on this continent in work of the sort. The United States Public Health Service has tentatively set 10 million particles per cubic foot (370 per c.c.) as the limit of safety in the case of granite dust. Merewether's figures range from 506 to 6324 particles per c.c. However, it is not strictly fair to compare the results obtained with 2 different types of apparatus.

It is the opinion of the author that continued exposure to high concentrations of asbestos dust may result in fully

developed fibrosis in 7 to 9 years, and possibly death in 13 years. The question as to whether asbestosis causes an increased susceptibility to tuberculosis remains uncertain.

K M Lynch and W A Smith (Am Rev Tuberc 23 643 (June) 1931) report a pure case of long standing asbestosis, with consequent extreme hyaline fibrosis of the lungs, obliteration of a large part of air-bearing tissue, emphysema, bronchiectasis, increased pulmonary resistance to the circulation, hypertrophy of the right heart with eventual degeneration, fibrosis and congestion of the heart, progressive heart failure, with generalized passive congestion of the viscera, and death from slow cardiac failure, the natural end-result of uncomplicated disease of the lungs of this extent and character. Of interest in the lung change was the presence of the common laminated hyaline fibrous nodule, which has been described heretofore as a characteristic of the fibrosis of pulmonary silicosis.

### ASPHYXIA NEONATORUM.

See NEWBORN, DISEASES OF

**ASTHMA.—ETIOLOGY.**—There continue to be found new exciting causes of allergic asthma. These reports will probably continue until every living and dead thing containing a distinctive protein has been found guilty. S J Parlato (J Allergy 1 307 (May) 1930) has convicted the sand fly (cad-dis fly), M A Ramirez (*Ibid* 1 149 (Jan) 1930) finds the pyrethrum flower, or chrysanthemum flower, a source of the malady, and J G Hopkins, R. W Benham and B M Kesten (J A M A 94:6 (Jan 4) 1390) believe the fungus *alternaria* to be responsible for asthma in a patient giving posi-

tive reactions to house dust containing the fungus *alternaria*.

**Heredity.**—G W Bray (Brit M J 1 384 (Mar 1) 1930) investigated 200 consecutive unselected cases of asthma with regard to sex incidence, age at onset of asthmatic symptoms, and the presence or absence of allergy in other members of the family. In all, 4152 relatives were considered. Only about 5 per cent of the children were of Jewish parentage. A positive family history of allergy was determined in 68.5 per cent of the cases. In 51.5 per cent the history was unilateral, while in 17 per cent, it was bilateral.

**PATHOLOGY.**—F L Weille (Arch Otolaryng 12 785 (Dec) 1930) removed 160 specimens of tissue from the nose and accessory sinuses of 26 patients with asthma or vasomotor rhinitis, or both, and examined the specimens macroscopically and microscopically. The most interesting macroscopic observation was the presence of occasional pus pockets in membranes from the sinuses. Microscopic examination disclosed metaplasia of the epithelium, thickening of the basement membrane, edema or fibrosis of the tunica propria, active mucous glands, and prominence of eosinophils. The findings showed that a thickened mucous lining of a sinus may contain a pus pocket constituting a source of focal infection.

G M Coates and M S Ersner (Arch Otolaryng 11 158 (Feb) 1930) found that the eosinophil is present in the mucous membrane of an asthmatic patient in conjunction with purulent conditions in the same membrane. Therefore, it seems logical to them to assume that the asthma and the eosinophil must be closely associated, as has been demonstrated by other studies on asthmatics.

**COMPLICATIONS —Heart.**—L Unger (J Allergy 2 17 (Nov) 1930) made a study which gives evidence that there is a definite damage or tendency toward damage to the heart in bronchial asthma. The diagnosis of true bronchial asthma was made in 74 cases by careful history, examination, blood count, Wassermann test, sputum, thorough skin tests, and chest x-rays. All doubtful cases, such as hypertension and decompensation, were excluded. Electrocardiograms demonstrated that the heart is damaged or tends to be damaged in a majority of all cases. Only 23 (31 per cent) were normal. The striking finding is the great frequency of a low R and high R, this must be considered as strongly suggesting that the heart is on its way toward right axis deviation as the result of right heart strain.

P. Vallery-Radot and G. Mauric (Bull et mém Soc méd d hôp de Paris 54 732 (Apr 28) 1930) report an instance of death during an attack of asthma in a woman, aged 40. After a long period of spasmodic coryza, attacks of bronchial asthma had appeared during the winter of 1927-1928. At first they were separated by long remissions but during the month of May, 1928, the attacks followed one another at short intervals. During the second half of the year 1929, the attacks diminished in intensity and frequency. At the time of admission to the hospital, September 28, 1929, the attacks were not particularly violent, the general condition was not disquieting, and the clinical examination did not reveal an important pulmonary or cardiac lesion. Nevertheless the patient died 3 days later, after an attack that lasted 26 hours and in which it was impossible to ameliorate the dyspnea.

A. M. Fisher and J. P. Beck (J Allergy 2 149 (Mar) 1931) present the case of a man, aged 32, with a typical history of asthma for 2 years. No definite allergic etiologic substance was found, but his allergy was thought to be bacterial in origin, and he apparently died of asphyxia during an acute attack. Small holes were found in both lungs with an escape of air into the pleural cavities, but without collapse of the lungs. The microscopic picture in the lungs was characteristic of that described in asthma, the chief pathologic changes being in the bronchioles, *viz*, plugging of the narrowed lumens of the bronchioles with thick mucus containing many eosinophils and Curschmann's spirals, great infolding of the mucosa of the bronchioles, a thickened hyalinized basement membrane, hypertrophy of the muscle wall, and infiltration of the mucosa, submucosa and mucous glands with many eosinophils and plasma cells. The tracheal mucosa contained a similar infiltration. There were also present marked emphysema and hypertrophy of the right ventricle.

C. Laubry (Bull et mém Soc méd d hôp de Paris 54 857 (May 26) 1930) reports that x-ray, electrocardiographic and clinical examinations revealed a normal heart in a patient, aged 50, who had had attacks of asthma since childhood. Several similar examinations made over a period of 2 years gave the same results and yet the patient suddenly succumbed during an attack. A second patient, whose condition was almost identical, succumbed similarly, presenting generalized cyanosis. The author gives as a possible explanation of the death, asphyxia, which might be due in some cases to bronchial obstruction but more likely in such sudden and fatal attacks, to respiratory pause, with



immediate and direct action on the heart

**Sinusitis in Asthmatic Children.**

P Chobot (Am J Dis Child 39 257 (Feb) 1930) states that the incidence of sinus infection in asthmatic and also in normal children is much higher than has heretofore been believed. In his series of 100 cases, 60 were boys and 40 were girls. The first attack occurred in the first year of life in 14 cases, in the second year in 19. These figures compare closely with reports of other observers. Of these patients, 15 had negative skin reactions. The incidence of the age of onset is parallel to that in hypersensitive patients. Fifteen per cent of the sensitive patients had their first attack in the first year and 23 per cent in the second year. The 15 negative cases in this series were studied, a positive family history being obtained in 5 children. Of the entire series, both sensitive and nonsensitive, 41 had sinus infections as demonstrated by x-ray examinations. Chobot recommends **conservative treatment** but he feels that **puncture and irrigation** should be performed *when conservative measures have failed*.

**Tuberculosis.**—Diaz C Jiménez (Rev españ de tuberc 1 1 (Apr) 1930) studied the relations between bronchial asthma and tuberculosis. He considers asthma as an allergic disease. He states that there is a condition of allergy in tuberculosis which favors the sensitization, first to the bacillary products from the tuberculous foci (which products act like allergens in the development of attacks of asthma), and then to some other external substance also. The greater number of asthmatic allergic patients are sensitive to a given substance, but in all of them a previous tuberculous allergy existed.

From his studies the author concludes that tuberculous allergy by itself may cause asthma. The association of asthma and tuberculosis is frequent in patients with intense allergy, small tuberculous lesions, and few toxic manifestations. Asthma of a pure tuberculous origin is uncommon. The results obtained with skin reactions, x-ray examinations, and examinations of the sputum, as well as those of tuberculin therapy, indicate that in 60 per cent of asthmatic patients tuberculous allergy is the factor that favors the sensitization to a new substance. The more advanced forms of tuberculosis, in which toxic and infectious phenomena are predominant and in which there are only slight manifestations of allergy, seldom appear in association with asthma. As a rule, there is an antagonism between the 2 conditions. In cases in which both conditions are present the aggravation of the tuberculosis stops the attacks of asthma, though they reappear if tuberculosis follows an improving evolution.

J Harkavy and S Hebal (Am Rev Tuberc 21 644 (May) 1930), in examining the protocols of 400 cases of bronchial asthma, found 40 cases in which there was clinical and x-ray evidence of pulmonary tuberculosis. All of these patients were ambulatory, and only 18 of the 40 attended the clinic with sufficient regularity to be studied. Of the 18, 17 showed chronic fibrotic tuberculosis with cavitation. The sputum of only 3 was positive for tubercle bacilli at some time before they came to the asthma clinic. Of these 18 patients, 9 proved to be insensitive and 9 were found to give evidence of protein hypersensitiveness by means of skin test. Six of these were studied by means of passive-transfer experiments and were found to have reagins in their serum for

some of the proteins to which they were susceptible. All in the protein-sensitive group were freed of asthmatic attacks by the removal of the offending proteins. The conclusion, therefore, seems reasonably justified that foreign proteins of the inhalant group and not the tubercle bacillus were responsible for the asthma in this group. Nine sensitive patients gave evidence of having foci of infection, 6 having chronic sinusitis, 2 bronchiectasis, and 1 a chronic focus of organized pneumonia. The asthma in this group is, therefore, to be ascribed to the complicating respiratory infection and not to the tubercle bacillus. This group of patients has done well during the summer months. In the winter they are subject to recurrent "colds," to which, in spite of operations on the sinus, they are not completely immune. In the authors' hands operative procedure in the presence of chronic hyperplastic sinusitis has been of no value whatever. Only patients with frank pus in their sinuses have derived any benefit from operative intervention. **Climatic change** has been of the greatest value.

**DIAGNOSIS.**—In a discussion of the diagnosis of asthma W. Z. Stewart (J Allergy 30 544, 1929) concludes that the size of a reaction does not indicate corresponding importance of clinical sensitiveness. An area of erythema in one patient may be just as significant as a wheal and erythema in another. The size of different reactions in the same individual is not indicative of relative clinical importance. Skin test reactions are often present after clinical hypersensitiveness has disappeared and they may represent past history rather than present illness. Many reactions to foods can be ignored when the major factors in the inhalant group have been eliminated.

**Basal Metabolism and Blood Calcium Studies.**—R. A. Kern and I. Teller (*Ibid* 2 488 (Sept.) 1931) have observed that patients with bronchial asthma frequently have a subnormal basal metabolic rate. This tendency seems to be even more marked in patients with allergic eczema.

There is a higher incidence both of thyroid enlargement and of a family history of goiter in asthmatic patients than in the average population which would seem to suggest that the lowered metabolic rate is due to a depressed thyroid function. There is evidence to show, however, that in most instances the lowered thyroid function is probably an effect, not a cause, of the allergic state.

Total blood calcium estimations in 75 patients with bronchial asthma were practically all within normal limits. The blood calcium level bore no relation to the type of asthma (allergic or infectious), to the presence or absence of active symptoms, or to the basal metabolic rate. The estimation of the total blood calcium percentage is of no value in bronchial asthma.

**TREATMENT.**—G. W. Bray (Arch Dis Childhood 5:237 (Aug.) 1930) urges, by way of *prophylaxis*, that intermarriage between allergiatics should be discouraged. Children of allergic parents should be watched from birth. Bronchitic attacks in eczema or prurigo children should be regarded as potential asthma; coughs should be quickly investigated, as well as sneezing, wet noses, or coryza on the slightest provocation. Furniture and bedding for these children should be of the simplest kind. An inhalant sensitization is acquired, kapok should substitute feathers or hair as bedding; furs and pets should be restricted. At the onset of any symp-

toms that may be of an allergic nature, thorough examination and testing both of the skin reactions and of the gastric contents should be advised. Septic foci, as teeth, adenoids and tonsils, should be remedied, and early breathing exercises and proper convalescence arranged after the infective diseases of childhood.

A. G. Auld (Lancet 1 804 (Apr 11) 1931) emphasizes the importance of **nonspecific treatment** in asthma. When the allergen is discovered, which is not often, specific treatment is best, but even in this case it is better to use also the nonspecific treatment for some time, as the patient may fall a victim to another allergen. Most patients who suffer from one allergen also suffer from others. **Peptone** and **serum peptone** are probably the best, as they do not cause anaphylaxis and are suitable for all cases, however much they differ, though in some cases they fail. The protease of the patient takes up the allergen and excretes it, which alone is a sufficient reason for the injection of peptone.

H. Petow and E. Wittkower (Klin Wchnschr 9 1712 (Sept 13) 1930) used **cutaneous tests** and **desensitization treatment** in 116 cases of bronchial asthma with the following results: 36 recovered completely, 34 were considerably improved, 21 showed temporary improvement, and 25 were not influenced. It was noted that the older the patient and the longer the asthma had existed, the poorer were the chances for recovery. Regarding the cutaneous tests, it is stated that they have been overvalued. Because nonspecific desensitization frequently brings satisfactory results, the practitioner may omit the complicated cutaneous tests. In cases that are refractory to treatment, cutaneous tests should be per-

formed in special institutes. If the specific allergen is known, it is advisable to remove it from the surroundings of the patient. This is the most effective treatment. In cases of hypersensitivity to dust, specific desensitization with dust extract has proved effective. If the specific allergen is not known, nonspecific desensitization with tuberculin or peptone gives favorable results in about 60 per cent of the cases.

J. Maxwell (Brit. M. J 1 854 (May 10) 1930) is convinced that **tuberculin** treatment is of value in a considerable number of cases of asthma which prove resistant to other therapeutic methods. It can be used in spasmodic asthma in patients of any age, and in careful hands is without harmful effect on the patient. To insure success it is essential that the course should be prolonged and, if necessary, it may be repeated. The results recorded compare favorably with those of other and more complicated methods of treatment and appear to justify its more general adoption, particularly in cases that do not yield readily to simple routine measures.

The treatment consists in the subcutaneous injection of increasing doses of old tuberculin in dilutions ranging from 1:1,000,000 to 1:100. The size of the initial dose depends on the results of the intradermal test. In all cases the injections are given weekly at first and the doses are cautiously increased, care being taken to avoid even local reactions. The usual method of increase when the weaker dilutions—from 1:10,000 to 1:1,000,000—are being employed, is to follow the initial 0.1 c.c. with 0.2, 0.4, and 0.6 c.c., proceeding thence to 0.1 c.c. of the dilution immediately stronger. The course is followed until the 1:1000 dilution is reached, and at this stage there are usu-

ally obvious signs of improvement in favorable cases. The interval between the injections is then increased to 2 weeks, and the dose is increased by 0.1 c.c. at each attendance until a maximum of 0.5 c.c. is attained. This dose may be repeated at monthly intervals as often as necessary. When the selected initial dose is 0.1 c.c. of the 1:1000 dilution—*i.e.*, in those patients who are not sensitive to tuberculin—the same dose is injected for 6 weeks and is then increased by increments of 0.1 to 0.5 c.c., this dose being repeated fortnightly as long as may be necessary. The maximum dose that has been given in this series is 0.4 c.c. of the 1:100 dilution.

E. L. Stern and C. A. Spivacks (J. Allergy 1:357 (May) 1930) noted that in a patient with bronchial asthma, stimulation of the sympathetic trunk between the level of the second and fourth intercostal spaces on the right side by an electric current, induced an attack of asthmatic breathing. On blocking this region with alcohol, the attack cleared up completely and almost immediately. Stimulation between the stellate ganglion and the level of the third intercostal space, after blocking of the levels at the second and fourth spaces, did not produce an attack of asthma. Several hours after the blocking on the right side, the patient was found to have a left unilateral asthma. Stimulation of the right sympathetic trunk from the level of the second to the fourth spaces caused dilatation of the right pupil. Blocking of the right sympathetic trunk by injections of alcohol, from the stellate ganglion to the region of the fourth thoracic ganglion, produced a Horner's syndrome of the right eye. Blocking of the right sympathetic from the stellate ganglion to the

region of the fourth thoracic ganglion, by means of alcohol injections, relieved a case of status asthmaticus for 1 month, *i.e.*, the patient, who had constant, repeated attacks of asthma, day and night, for about 3 weeks previous to the injections, had virtually no asthmatic attacks of any severity, and the lungs were clear for almost an entire month after the injections.

V. Zipperlen (Strahlentherapie 36:88 (Mar.) 1930) reports the results of a follow-up study of 54 persons who one year or more previously had been given x-ray irradiations of the chest and spleen for bronchial asthma. He found that 9 did not show improvement, 15 had fewer and less severe attacks, 15 had attacks only at intervals of several months, and 15 were cured.

#### TREATMENT IN CHILDREN.

—M. M. Peshkin (Am. J. Dis. Child 39:774 (Apr.) 1930) analyzed a series of 425 cases of asthma. He found that in 41 children, ranging in age from 2 to 14 years, or approximately 10 per cent, the asthma remained severe, persistent, and of long duration, in spite of intensive modern treatment. Twenty-five children (22 sensitive and 3 nonsensitive to protein) were treated by a **change of environment**. In spite of the fact that the inhalant and the dietetic restrictions were kept less rigid than at home, 23 children, or 92 per cent, were markedly improved or entirely relieved of asthma. Of these 41 children, 16 were not treated by a change of environment because of lack of facilities and other reasons and so indirectly served as a control series. These children are still suffering from chronic asthma. The author feels that until newer methods of treatment are advanced that will successfully control or free this group of children from asthma, the establishment of a "home"

where a child with chronic refractory asthma can be kept for at least 6 months is regarded as a humane, urgent and economic necessity, as well as a therapeutic measure of definite value

M M Peshkin and A H Fineman (Am J Dis Child 39 1240 (June) 1930) relate that in 15 children, from 3 to 15 years of age, of whom 12 were sensitive and 3 were nonsensitive to protein, the asthma remained severe, persistent and of long duration in spite of treatment according to accepted standards of modern investigation and management. These children had been under observation for an average of  $2\frac{1}{2}$  years when selected for treatment with the **ketogenic diets**. No drugs, injections or other therapeutic measures were used. All foods recognized as possible causes of allergy in these patients were eliminated not only from the former diets, but also from the ketogenic diets.

An estimation of the amount of food consumed by these children before the beginning of the ketogenic diet showed that they were all living on a high carbohydrate diet. Average approximate ketogenic-antiketogenic ratio of the home diets ranged from 1 to 2 to 1 to 3. A maintenance diet or one of higher caloric value with a maximum ketogenic ratio of 3 to 1 was reached in all cases except one within 3 weeks, and after that the level was maintained for periods ranging from 4 to 10 months. At the end of the third week of treatment 14 children, or 93 per cent, showed marked improvement or relief from asthma. Improvement was maintained for 2 months. After that and up to the tenth month, 53 per cent were considered moderately to markedly improved or relieved from asthma.

The ketogenic and low-carbohydrate diets alone do not appear to offer much

promise of relief from pollen asthma or hay-fever. In *pollen asthma* the administration of **pollen treatment** in conjunction with the **ketogenic diet** may prove of value. The results obtained cannot be ascribed to ketosis, as definite improvement or relief from asthma occurred in some children in whom acetone in the urine could not be demonstrated. The use of a maintenance diet or one of higher caloric value with a ketogenic ratio of 3 to 1 in the treatment of a child with chronic asthma who is underweight usually results in an appreciable gain in weight after a period of 4 months, while in a child who is obese the use of this diet usually results in a loss of weight, in spite of the fact that both types of children have been improved or relieved from asthma.

Children with asthma and recurrent eczema on a ketogenic diet showed definite improvement from asthma but aggravation of the eczema. Children who had been free from eczema for several years prior to the institution of the low-carbohydrate-high-fat diet, did not have a recurrence of the rash in spite of the prolonged ketosis.

The estimation of the requirement in any given case was more easily determined from the formula of Pirquet. The food requirement is calculated by multiplying the square of the sitting height in centimeters by the desired number of decinems. Multiplying by two-thirds, the number of calories is obtained. The maintenance diet is calculated at 4.5 decinems and a basal requirement at 3 decinems.

The rapid control of asthma or relief from it resulting from the ketogenic diet possibly is brought about by some mechanism which involves a physiochemical change in the cells and blood of the patient, thereby inducing a par-

tially or completely restored physiochemical or allergic balance

A A Osman (Lancet 2 1187 (Dec 7) 1929) found that an increased allowance of **sugar**, as such (*ie*, not as starchy foods), in the diet alone was sufficient to prevent recurrence of asthma in 4 children over a considerable period. The treatment consisted in giving 3 drams (12 Gm) of **powdered dextrose in lemonade** 3 times a day, in between meals, with extra sugar and "sweets". In each case this treatment resulted in a marked improvement in the general health and spirits, in addition to the complete disappearance of the asthma. No evidence has been obtained as to the mode of action of sugar in these cases, but the author is inclined to attribute its beneficial effects to the improvement in the general health.

R A Kern (M Clin. North America 12 1085 (Jan) 1929) states that the commoner errors in handling asthmatic patients are failure to avoid the offending substance to which the patient is sensitive and the inadequate treatment of sinus disease, that relapses are mostly traceable to reexposure to old causes, to the development of new, sensitizations, to reinfection, and to progressive nasal pathology, and that the patient whose disease has relapsed should be studied just as if he were a new case.

**ATELECTASIS.**—E Korol (U. S. Vet Bur M Bull 7 10 (Jan) 1931) describes 10 cases: 3 of aortic aneurism, 2 of mediastinal tumor, 2 of leukemia, 2 of Hodgkin's disease involving the mediastinal or hilar glands, and 1 of postoperative massive atelectasis. In certain cases treated by x-rays or radium, the signs of atelectasis disappeared, following a diminution of the size of the mediastinal masses. A short review of

the literature indicates that aneurism and mediastinal tumor have been recognized as causes of atelectasis, but there are no references to atelectasis accompanying Hodgkin's disease and leukemia. The occurrence of bronchiectasis in atelectasis is discussed, including the symptom-complex resulting from interference with bronchial drainage.

**POSTOPERATIVE.**—A L Brown (Arch Surg 22 976 (June) 1931) stresses the importance of the bronchial secretions in producing postoperative atelectasis and in determining the specific type of atelectasis that ensues. He has noted both experimentally and clinically that thick, tenacious sputum plugs the larger bronchi, whereas thinner sputum tends to greater dispersion and a blocking of the finer bronchi and bronchioles, thereby producing a scattered lobular atelectasis. At first thought, it may be imagined that postoperative pulmonary atelectasis might occur more frequently following inhalation anesthesia than following spinal anesthesia. But on closer consideration, several reasons are noted why spinal anesthesia might predispose to this complication, *viz* (1) Spinal anesthesia definitely inhibits the depth and force of respiratory movements, not only during the operation itself but for a considerable period thereafter. It is these respiratory movements (both intrinsic and extrinsic) that tend to rid the tracheobronchial tree of foreign matter or secretions. (2) The normal viscosity of the secretions of the tracheobronchial tree appears to be increased: *ie*, the material is more tenacious following spinal anesthesia. (3) Following operation under spinal anesthesia, the patient tends to remain relatively quiet for a number of hours. There is, then, a more tenacious sputum and decreased or impaired factors that might



tend to free the tracheobronchial tree from this material. The increased possibility for this material to obstruct or plug a bronchus and the subsequent development of atelectasis appear reasonable. The author is under the impression that spinal anesthesia predisposes to postoperative pulmonary atelectasis.

**MASSIVE PULMONARY.**—By extensive experimental work some of the underlying problems of massive collapse are being brought nearer solution. That bronchial obstruction is necessary to collapse appears proven by P. N. Coryllos and G. L. Birnbaum (*Arch Surg* 21 1214 (Dec) (pt 2) 1930). Emphasis is laid on the experimental findings that massive collapse took place only when the obstruction was of the lobe bronchus and did not occur when a secondary bronchus was the seat of the occlusion produced, this being entirely independent of the type of breathing in the experimental animal. Moreover, that absorption of alveolar air in lobar obstruction occurred by way of the circulating blood was proven by the repeated introduction of air and other gases into the alveolar system distal to the bronchial obstruction—with the dog in the observation negative chamber—and the reinflation of the collapsed lung observed on the one hand and recurrence of atelectasis at regular time interval as absorption again took place.

These authors further observed that violent expulsive cough efforts will hasten collapse where the obstruction is of the expiration valve type, as indicated by their findings that if a part of the entrapped alveolar air is aspirated through the cannula, atelectasis will occur more rapidly, the time being inversely proportional to the amount of air extracted.

That the maintenance of a pulmonary

circulation is essential in the production of atelectasis they believe because

"If the branch of the pulmonary artery corresponding to the obstructed lung is ligated, atelectasis will not occur. As a matter of fact, after this ligature the lung shrinks a little, and after several days becomes quite airless for weeks because of fibrotic contraction. The fact to keep in mind is, as Lichtheim long ago proved, that obstruction of a bronchus does not lead to atelectasis unless the circulation is intact."

If after atelectasis has occurred air is again introduced into the atelectatic lung, not only does it regain its previous appearance, but also the same cycle of phenomena begins again, *i e*, qualitative and quantitative changes in the entrapped air and the production of atelectasis in the same length of time if other conditions (general condition of the animal, circulation, respiration, etc) remain the same.

Explanation of discrepancies in experimental findings, at first apparently completely contradictory, where bronchial obstruction was produced is now proven to be due to rapid passage of gases from lobule to lobule, through the alveolar walls themselves, accounting for failure of production of atelectasis experimentally when the obstruction of the main bronchus itself was not complete. This has been well and simply verified by W. E. Adams and H. M. Livingstone (*Arch Surg* 23 500 (Sept) 1931), who produced stenosis, cicatricial and localized, by the use of 50 per cent silver nitrate. They observed that if at autopsy the primary bronchus of a lobe was found to be completely stenosed, this condition was accompanied by massive collapse (100 per cent) of the obstructed pulmonary lobe. However, if the stenosis was all

but complete, with an opening of only 1 mm remaining, no atelectasis resulted. The lobe appeared normal both on gross and microscopic examination.

On the other hand when the bronchoscopically controlled cauterization was limited to the secondary lobe bronchi they report one protocol as follows, stating that the identical findings were recognized in 10 experiments. "At autopsy, the lateral secondary bronchus to the lower right lobe was completely stenosed, with the air-passages distal to the stenosis dilated and filled with a mucogelatinous material, the retained secretion from the mucus glands. The medial secondary bronchus was markedly but not completely stenosed, an opening of 1 to 2 mm. remaining. There was no dilatation distal to this complete stenosis. The entire lobe was completely air containing on external examination and on cut section. Pieces floated on the surface when placed in water. Microscopic section showed the alveoli to be air containing." Various lobes of the lung were used (in the 10 experiments) with like results being obtained with regularity. Thus, complete obstruction of the air passages of only a part of a lobe was not followed by massive collapse. Only a dilatation of the larger air passages distal to the stenosis, resulted, with the alveoli normally air containing.

Whether the air or other gases pass through the alveolar wall by diffusion or through actual "pores" is a point of discussion. C. M. Van Allen and G. E. Lindskog (Arch Surg 21. 1195 (Dec) (pt 2) 1930) believe the fact that a particulate substance is admitted indicates that there must be anatomic connections. These are evidently in the periphery of the lung, and they may be the alveolar wall pores recently de-

scribed by Ogawa as to position, shape and construction. It has been found that an obstructed portion of one lobe breathes by means of communication through adjacent free parts, and that the amount of this respiratory interchange may be as much as 3600 cc per hour. It fails to occur between lobes.

Coryllos (*loc cit*) states that the alveolar "holes" (*trous d'usure*, Letulle) were known and carefully studied a long time ago. The majority tend to believe that the pores generally occur in the lungs of elderly subjects and that they are the result of a wear and tear process. Whatever they may be, these pores are not essential for the explanation of the phenomenon because the interalveolar septums are perfectly permeable to gases. This can be shown by insufflating 100 per cent ether vapor into the alveoli through the obstructing cannula. The passage of air ceases immediately because of the edema of the interalveolar septums caused by the ether. This explains why "patchy" atelectasis is possible only in the presence of some degree of inflammatory edema of the alveolar endothelium. In a healthy lung patchy atelectasis would be little short of impossible, because exchange of gases continues through the interalveolar septums even when the alveolar duct is completely obstructed.

The practical clinical value of these conclusions, applicable in prevention and treatment of atelectasis, lies in the advantage of free breathing which, by opening up partially obstructed bronchial passages, and the reserve alveoli not ordinarily in use, favor this diffusion, and provide the "available air" in the alveoli behind the obstruction, utilizable to force out the plug by coughing efforts.

As to the clinical application, Van Allen and Lindskog (*loc cit*) consider that another circumstance of great importance requires attention, *ie*, the infection that precedes and accompanies atelectasis in most instances. Bacterial or chemical inflammation of the bronchi is usually responsible for obstructive secretions and exudates, and to infection are due in large part the distressing symptoms and dangerous complications of atelectasis. That the dyspnea, fever and prostration are immediately related to the infection, rather than to the collapse of the lung, is strongly suggested by the facts that compressive atelectasis, as in pneumothorax, produces relatively slight cardiorespiratory disturbance and no toxemia, and that obstructive atelectasis in the dog does not give rise regularly to any of these effects. The loss of function of so much lung is probably of no importance in itself in most cases.

**PROPHYLAXIS.**—Care should be taken also not to aggravate the accompanying infection. Indeed, conservatism may well be indulged in for the present, as atelectasis in massive proportions is unusual, its morbidity brief, and fatality from the condition itself rare.

Fluids accumulating in the bronchial tree tend to settle first of all in the smaller passages, and the earliest total obstruction is likely to be lobular. At this stage it should be possible to prevent collapse of the lung in the obstructed parts by maintaining aeration. This may be done by an occasional deep breath. Coughing should be used in moderation, since its action is not always effective, and may be harmful. Excessive spontaneous coughing should be controlled.

**Elevation of the foot of the bed** is the only constant addition to the ordinary nursing and general supportive

measures. If it is evident that bronchial secretions are excessive, a regular schedule is adopted, with a change of side in the lying position and with encouragement to inspire deeply and to cough once or twice at hourly or half-hourly intervals. In sleeping, unconscious or otherwise uncooperative patients, inhalations of carbon dioxide should be substituted.

**TREATMENT.**—Once physical signs and symptoms indicate that atelectasis has occurred, the above measures, if not already in use, are instituted. **Bronchoscopic aspiration** has a place in the treatment, for in numerous reported cases the lung has returned to normal x-ray appearance and symptoms have disappeared after removal of mucus from the bronchi. However, bronchoscopic treatment is not always available, so that other measures that have proven beneficial must be used when a bronchoscopist is not at hand, *viz*, frequent change of posture, dependent drainage by lowering the head of the patient, increase in depth of respiration by the use of carbon dioxide at intervals, with encouragement of cough in moderation.

**ATROPINE. — PHYSIOLOGICAL ACTION.**—The action of atropine on the *bile ducts* in the human being was studied by the means of duodenal intubation and cholecystography in the laboratory of A. Grebe (Ztschr f klin Med 115 446 (Feb 12) 1931). Before the administration of atropine, the bile could not be obtained from the gall-bladder during a few hours following evacuation of the bile with the tube. Following the administration of 1 or 1.5 mg ( $\frac{1}{64}$  or  $\frac{1}{40}$  grain) of atropine the gall-bladder appeared filled with bile during that time, the amount and con-

centration seemed to be increased. Under the influence of atropine, evidently the passage of bile into the gall-bladder is more rapid and more complete. These opinions were confirmed on colored cholecystographic examination. The shadow of the gall-bladder appeared larger and more intense about 5 hours after oral administration of atropine. Evacuation of the bile was held up as long as the action of atropine was present, but in this time the use of stimulating remedies was of no avail. Sometimes a sudden escape of bile occurred as the result of a spontaneous contraction. After 4 or 5 hours, however, an enhanced evacuation of the bile appeared. This was present in cases in which there was disturbed evacuation of the bile, as in cases of peptic ulcer and dyskinetic disturbances of the gall-bladder. As before, the results obtained in this manner agreed with those of cholecystographic examination.

As a result of their researches S. Amberg and O. Grob (*Am J Dis Child* 41:507 (Mar) 1931), state that the pressure of the *urinary bladder* in the child may be lowered after the administration of atropine. This agent also exercises an influence on the amplitude and frequency of the bladder contraction. So far, the effect of atropine was studied only insofar as it had any influence on patients with enuresis, *i e*, a disorder of micturition, and it has been obtained only in a certain number of cases. In the majority of cases ob-

served by these investigators, atropine produced primary, although transitory, slowing of the pulse rate which was followed, however, by a period of acceleration. The action of this drug on the bladder was not dependent on, or related to, the usual action of atropine on the eye, skin, mucous membrane and pulse.

The synergistic action of atropine and epinephrin on intrinsic *muscles of the eye* was studied by H. Hartgraves and P. C. Kronfeld (*Arch Ophth* 5:212 (Feb) 1931). They believe that epinephrin in the dosage that was used in the cases under their observation has no influence on the tonicity of the ciliary muscle of the eye, and, therefore, no noticeable influence on the static refraction of the eye, although the range of accommodation is considerably reduced. Epinephrin and cocaine, therefore, are cycloplegics which prevent, or in smaller doses only reduce, the contractility of the ciliary muscle, but do not change its original natural tone. For atropine, the observation still is true that it produces the maximum possible relaxation of the ciliary muscle and so the minimum static refraction known thus far. The failure of the sympathomimetic drugs to increase the effect of atropine indicates that the effect of the latter on the ciliary muscle cannot be increased by any method known to date.

**AVERTIN.** See ANESTHESIA, BASAL

## B

**BACTERIOPHAGE.** — Bacteriophage is destined to revolutionize the entire science of bacteriology, pathology, prevention and treatment of all infectious diseases if the opinion of F d'Herelle is correct (Bull et mém Soc nat de chir 56 986 (July 19) 1930). In reviewing his own work, d'Herelle states that coincident with the onset of convalescence from numerous intestinal infections, a lytic principle appears in the intestinal tract which possesses the ability of destroying and dissolving pathogenic bacteria. In later observations, the author noted that this phenomenon accompanied other diseases than bacillary dysentery, such as cholera, typhoid fever, infantile diarrhea, human and animal septicemias, and bubonic plague. During convalescence from all of these affections there is a bacteriophagic principle possessing the power of destroying and dissolving the pathogenic bacteria concerned in the production of that particular infection present.

The process of destruction of these pathogenic organisms by the bacteriophage, when regarded microscopically, is that of a sudden bursting, the body of the bacterium swelling little by little and then suddenly rupturing, leaving nothing that is visible. D'Herelle concludes that bacteriophage is in the nature of a corpuscle about 10 millimicrons in diameter, and that it multiplies very rapidly at the expense of the specific bacteria.

The bacteriophagic corpuscle acts apparently on the bacteria by means of a ferment. Secretion of a soluble ferment implies of course the existence of a metabolism in the organisms; therefore, the bacteriophage is regarded as a living virus or a bacterial parasite

and the disease of bacteria caused by the bacteriophage may then be designated *bacteriophagia*. This is but another example of the general and accepted biological phenomenon of parasitism.

Some of the bacteriophagic principles are specific; others exhibit a group action. For example, some attack the *Bacillus coli*, *Bacillus dysenteriae*, vibrio of cholera, while others are specific for the *Bacillus coli*, *Bacillus pestis*, and *Bacillus typhosus*. They all vary considerably in the intensity of their action, some being weak and others strong. Bacteriophage is present from a few days after birth in the intestinal tract of all living beings from molluscs to man, and multiplies at the expense of *Bacillus coli*. It can adapt itself to act as a parasite against bacteria which it was at first unable to attack. As this power of adaptation varies considerably, the principle of treatment with bacteriophage consists in injecting into a diseased individual a phage which has heretofore become accustomed to living as a parasite on the microorganism which has caused the affection.

In other diseases which are non-intestinal in character, such as septicemias, and bubonic plague, d'Herelle has been able in every case to isolate a phage from the diseased tissue, buboes or blood, at the onset of the illness. From d'Herelle's original work, he concludes that recovery from an infected disease is due to the action of a bacteriophage *in vivo*, rather than to the production of immunity, and he states that immunity follows recovery and does not precede it. Since the possibility of relapse frequently exists, it indicates that true immunity is established cer-

tainly not before, but several days after the onset of convalescence. In cases previously treated with vaccines and antisera, the action of bacteriophage is apt to be slower and sometimes absolutely of no avail, and for this reason, the investigator believes that bacteriophage should be used to the exclusion of other biological preparations.

In a further discussion d'Herelle (Canad M A J 24 619 (May) 1931) points out that recovery from an infectious disease cannot be the consequence of an acquired immunity, and finds that all the infectious diseases, as well as the pyogenic infections, are not immunizing. In the case of those diseases which produce active immunity, however, if recovery does take place from the acquisition of immunity, d'Herelle questions how the relapses occasionally noted during convalescence at the moment when the immunity should be most potent can be explained satisfactorily. He finds, therefore, that antibodies do not provoke the recovery and, further, that immunity was not yet established at the moment of the recovery from the original attack. He states now that recovery can take place without the phenomenon of immunity, and that acquired immunity, not being the cause of the recovery, appears from 10 to 20 days after recovery.

The noteworthy findings in d'Herelle's experiments have been the appearance within the body of the patient of the principle leading to bacteriophagy coinciding with the time when amelioration of symptoms takes place. While it is absent during the disease, bacteriophage is always present in convalescence and, therefore, contemporaneous with recovery. Numerous observations indicate that the bacteriophage exists in corpuscular form, it being a living ultra-microscopic organism, as indicated by

the fact that this corpuscle dissolves bacteria through the agency of a ferment which it secretes. There are races of bacteriophage capable of attacking many species of bacteria, while others attack but a single species or even but a single bacterial strain. Certain of them, however, are so strong that they are able *in vitro* to destroy and dissolve within less than 2 hours all the bacteria contained in a culture, whereas others may show a scarcely perceptible, partial action.

P Hadley and B Jimenez (J Infect. Dis 48 176 (Feb) 1931) performed a test showing that the essential prerequisite for development of bacteriophage in a pure line culture is not other bacteriophage from an external source, but something that may be designated, for the want of a more suitable term, the "liberating stimulus" or "incitant." At the present time, it is important to differentiate carefully between the indefinite stimulus that serves first to liberate bacteriophage in a culture and the definite units through the activity of which the lytic properties become transmissible. Either of these influences, used in conjunction with an alkaline medium, can force the cells of the culture into a new direction of growth (dissociation) or possibly compel them to employ another mode of reproduction in order to sustain life.

The influence of pus, blood, blood corpuscles and blood serum on the activity of bacteriophage *in vitro* was studied by M Applebaum and W. J. MacNeal (J Infect Dis 49:225 (Sept.) 1931). A purulent exudate shows a marked inhibitory influence on the lytic action of the antistaphylococcus bacteriophage sufficient to explain the persistent survival of the bacteria in purulent collections within the body of a patient re-



ceiving treatment with potent bacteriophage. Even diluted 1:1000, a purulent exudate occasionally shows a relative inhibitory effect *in vitro*. By heating the pus to 60° C for ½ hour, the inhibitory effect was only slightly diminished. Similar dilutions of purulent material failed to exhibit any analogous inhibitory effect on the lytic action of the anticolon bacillus bacteriophage. Undiluted citrated blood, undiluted defibrinated blood and diluted serum show an inhibitory influence on the antistaphylococcus bacteriophage, but there is considerable variation of different bacterial strains and of the different races of bacteriophage. Experiments with diluted serum failed to show any clearly evident inhibition of the anticolon bacillus bacteriophage, but undiluted blood does not permit the multiplication of the colon bacillus under the experimental conditions used by Applebaum and MacNeal.

**LIMITATIONS.**—In an editorial (J. A. M. A. 96:693 (Feb 28) 1931) entitled "Limitations of Bacteriophage Therapy," it is stated that the d'Herelle phenomenon has been the subject of more than 2000 papers published since this was first described by Twort in 1915. In this immense amount of literature but little unanimity of opinion has been noted concerning the mechanism of action of bacteriophage, and no reliable guide to the practical limitations of therapy by its use is available. The lack of a dependable quantitative method is the chief factor causing this uncertainty.

A. P. Krueger (J. General Physiol. 13:557 (May) 1930) devised a quantitative technic by which the phage could be estimated with an accuracy of plus or minus 3 per cent, and with this technic, A. P. Krueger and J. H.

Northrop (*Ibid* 14:223 (Nov) 1930) observed the kinetics of the bacterium-bacteriophage mixture. Their findings would indicate that future therapy must be limited to certain definite anatomic types of infection, and that the theories of the future must be laid along different lines. They found no evidence that supported the hypothesis that bacteriophage is a living biologic entity. During the stages before explosive bacterial lysis takes place, Krueger and Northrop found no evidence that ordinary amounts of bacteriophage had any influence whatsoever on the bacteria, neither stimulating nor retarding growth. They found that the elaboration of this lysin is intimately associated with the growth of the bacteria, and the bacteriophage is formed within the bacterial cells and diffuses outward at such a rate that extracellular concentration and intracellular concentration of bacteriophage maintain to each other a constant mathematical ratio. This diffusion is common to simple chemical solutions but would hardly be looked for were the bacteriophage a living particle. At a point when the critical ratio between bacterium and extracellular bacteriophage is attained, bacterial multiplication ceases and bacterial dissolution begins.

Mathematical formula has been elaborated by Krueger and Northrop (*loc. cit*) by which they can accurately predict all the major events of this relationship, including the rate of bacterial growth of bacteriophage formation, time of lysis, and concentration necessary for bacteriostasis, showing that a certain critical concentration of extracellular bacteriophage is necessary for bacteriolysis to take place, and in about the same way that a critical environmental carbon dioxide concentra-

tion is necessary for death from carbon dioxide autointoxication. As the editorial points out, this signifies that no therapeutic effects are predictable for bacteriophage, except under the conditions in which local extrabacterial bacteriophage concentration can be produced and maintained at a critical level, which may be accomplished either by direct use of massive doses of phage or by allowing free bacterial growth in the presence of smaller doses. It is hardly to be expected that such a critical extrabacterial concentration could be produced in any tissue in which extracellular bacteriophage is denatured, bound, removed or diluted by the circulation of the blood or lymph or urinary secretion. Therefore, bacteriophage therapy is said to be a predictable disappointment in erysipelas, furunculosis, pneumonia, pyelitis, cellulitis and bacteremia, and in cystitis except by concentrated irrigation. The value of this treatment would be limited to its use in closed organs as the intestine and to well encapsulated pus cavities. As this editorial points out, if the bacteriophage might prove the method of choice in but one of these affections, the work on this phenomenon during the last 15 years would be well worth while.

**THERAPEUTICS.**—The variability in the therapeutic effects of bacteriophage is due to several factors. As pointed out by F. B. Lynch (*Am. J. Clin. Path.* 1:449 (Nov.) 1931), the accessibility of the pathologic focus to the bacteriophage filtrate is of first importance, then, if a bacteriophage does not totally destroy a culture, the organisms that survive may produce a resistant strain of organisms which may be pathogenic for the host but unaffected by the bacteriophage. A bacteriophage for staphylococcus infection is available

which is lytic for practically all strains of staphylococci and is so strong as to destroy numerous strains without the development of resistant forms. On the other hand, however, resistant strains of colon, typhoid and dysentery bacilli develop much more promptly. Only young cultures of most of the strains of these bacteria are susceptible of complete lysis, while the older bacteria become the progenitors of resistant strains.

In blood borne infections, bacteriophage does not appear to be so potent, because of the adsorption of the phage by the blood serum colloids. The bacteriophage in some vaguely understood way, sometimes frees itself of the colloid and localizes at the site of the infection. Experimentally, with certain infections, as peritonitis, in order to obtain the bacteriophage action, it must be injected not later than a half-hour after bacterial inoculations. This phenomenon cannot be fulfilled in clinical practice and with these infections, therefore, the use of bacteriophage seems to be limited to prophylaxis. In a bacteriophage filtrate, the protein present seems to have an important bearing on the dosage and method of choice for administration. It is obtained from the extractives in the culture mediums, and from the bacterial protein of the lysed organisms. If it is desired to give bacteriophage orally, as in cholera, typhoid or dysentery, the amount of protein present in a dose of 2 to 10 c.c. is of no consequence; but if the phage is to be injected intravenously, the amount of peptone and bacterial protein in the filtrate is of primary importance. This is true to a lesser degree of subcutaneous or intramuscular administration. Occasionally an extensive local reaction may follow a dose of too highly concentrated

bacterial protein. Lynch states that the choice of administration for cholera, typhoid, dysentery and similar affections is the oral route. When the bacteriophage is so administered, it causes no development of an antibacteriophage, which is of considerable value.

Two to 5 c.c. of an active phage filtrate may be administered over a period of 7 to 10 days daily. For wound infections, wet dressings of bacteriophage occasionally produce a spectacular result, and Lynch states that he has seen this in both staphylococcal and colon bacillus infections. He advises that 1 to 4 c.c. of bacteriophage solution be poured into the wound and a wet dressing of physiologic saline solution be applied.

The subcutaneous route is probably the most common manner of administration. The intravenous method is not ordinarily advocated because of the adsorption of bacteriophage by the serum colloid. The filtrate may be injected directly into the lesion but, at least in certain experimental infections, it may act on a distant focus. Bacteriophage has been injected directly into and around a boil or carbuncle, the dose varying from 0.1 to 1 c.c. as required. For cases of pyelitis, the method of choice is irrigation of the bladder and of the renal pelvis.

If there is no lysis *in vitro*, no lysis *in vivo* will take place, as pointed out by P. Hauduroy (Presse méd. 39:168 (Feb 4) 1931), who further states that it is best to prepare the bacteriophage with the patient's own bacteria. This investigator has treated infections by staphylococcus, colon bacilli, and typhoid bacteria with bacteriophage. He advocates 3 or 4 subcutaneous injections of 2 or 3 c.c., each administered at intervals of 24 hours. He states that these

injections only rarely cause a slight local reaction and never produce a general reaction. He obtains better results when the injections are given at a point distant from the original focus of infection.

In no event, should more than 5 injections be administered, since more than this number will sensitize the organism and possibly stir up the infection. When accessible, the lesion should be directly treated with a bacteriophage dressing. This procedure is never painful. Where an abscess on the body surface is found, a bacteriophage compress should be applied.

Hauduroy advises against intravenous injections. He has obtained good results in all superficial or deep staphylococcal infections, as furunculosis, anthrax, abscess, dermatitis, and pyodermitis, caused by the staphylococcus, but staphylococcus septicemia on the other hand does not appear to be benefited. Four cases treated by the author showed disappointing results.

When successful, improvement is noted after 2 or 3 days of treatment. The open lesions are promptly emptied and the pus flows out freely. Fluctuating lesions open and undeveloped lesions may retrogress entirely. If the suppuration has not disappeared within a week or 10 days, this form of treatment has failed. Hauduroy finds that about 75 per cent of cases with staphylococcus infection are cured.

As the occurrence of lysis was shown *in vitro* before the treatment in every case, failures may have been from sensitization of the organism. When staphylococcus bacteriophage applied alone was not sufficient, Hauduroy has supplemented this treatment by an injection of vaccine after each subcutaneous injection of bacteriophage. For

infections due to the colon bacillus, the phage treatment will produce a cure only if the infection is uncomplicated

In many of the cases showing an enterorenal syndrome and in cases of obscure origin of enteritis or dysentery, the bacteriophage orally administered frequently produces satisfying end-results, because the phage appears to restore the intestinal flora to normal.

Treatment of typhoid fever with bacteriophage has been disappointing in the hands of Hauduroy. Although he quotes Breton, who claims to have obtained a cure in 3 cases by giving bacteriophage intravenously, the present author, however, considers that the cure was due to the severe shock caused by the injection.

Various dilutions of bacteriophage and several chemical disinfectants were mixed with a definite quantity of staphylococci and injected into rabbits intracutaneously by J. E. Walker (J. Infect. Dis. 46:324 (Apr.) 1930), who examined the resulting lesions. He used mercuric chloride, phenol, formaldehyde, tincture of iodine, and chloramine, and found that staphylococcus bacteriophage had a much wider range of dilutions (from full strength to 1:512) over which the resulting lesions were partially suppressed without necrosis of the cells. The chemical most nearly approximating in this respect was mercuric chloride, which when diluted to one-sixteenth of the strength causing necrosis, would partially suppress the staphylococcus bacteria. From these results Walker concludes that bacteriophage is a more suitable local dressing than the chemicals for staphylococcus infections.

The bacteriophage therapy was tried by G. Pacetto (Políclinico (sez. chir.) 38:76 (Feb. 15) 1931) in 36 cases of

carbuncle, furuncles, hidrosadenitis, abscess, phlegmon and mastitis. In 88.2 per cent a cure was accomplished, in 2 to 10 days, with from 1 to 3 injections of the bacteriophage, while in 11.8 per cent, a suppurative process resisted phage treatment and surgical intervention was required. No instances of exacerbation from the use of bacteriophage therapy was noted by this observer.

A. Liengme (Rev. méd. de la Suisse Rom. 51:482 (June 25) 1931) supports d'Herelle's contention that bacteriophage is a powerful therapeutic agent in infections. This author states that the indications for phage are based on the fact that it is necessary to obtain an autobacteriophage. The best results are obtained from local infections. This observer recommends bacteriophage as an ideal therapeutic measure, since it is not accompanied by toxic action on the cells and does not produce any reaction. Depending upon the clinical findings and the action of the bacteriophage, cure may be looked for in from 1 to 8 days after institution of phage therapy. When large losses of substance have occurred from destructive necrosis, more time may be necessary for the wound to close. Nevertheless, even with these cases Liengme obtained a cure. All that is necessary is to wait for cicatrization to take place. At times, a polyvalent bacteriophage may be required as a prophylactic measure in contaminated accidental wounds.

Bacteriophage in surgery is discussed by F. H. Albee (Internat. J. Med. and Surg. 43:461 (Sept.) 1930), who compares it with the modern treatment of osteomyelitis advocated by Orr, which, instead of using frequent dressings and almost daily interference, permits the wound to remain for weeks or

months without interference, allowing the products of the bacteria as well as the granulations to remain undisturbed in contact with the wound. This seems to induce a native bacteriophage which, when absent, is accompanied by a delayed healing and when present accelerates the healing. Antiseptics may destroy the bacteriophage.

The appearance of granulations in a wound treated by this procedure is most characteristic, being glistening red and not exuberant or edematous. When well packed with vaseline gauze and enclosed in a dressing surrounded by plaster, so that uniform pressure is exerted upon it and the surrounding tissues, the normal appearance of the resulting granulations indicate that normal physiological pressure has been brought about by the dressing. The pus is expressed and the packing extruded from the wound by pressure of the growing tissues. The optimal point for healing of the tissues is that at which the equilibrium is maintained by the dressing. The healing of the wound is greatly favored by the equalization of the pressure at an optimal level at which the speed of epithelialization is greater, as noted in the treatment of varicose ulcers. Albee in the past 3 years has treated more than 150 cases by this closed method satisfactorily.

Various diseases of the nasopharynx were treated by autobacteriophage and Besredka's antiviral by E. Théobalt and R. Moline (*Presse méd* 39.1417 (Sept. 26) 1931). The 2 preparations were in sealed ampules and used simultaneously or alternately as required. In rhinitis, instillations and nasal dressings were used. Plugs of gauze or absorbent cotton moist with the bacteriologic preparations were introduced

with a speculum and placed in contact with the middle and lower turbinated bones of both sides of the nose. No anesthesia was necessary, cocaine was regarded as hindering the adsorption of the antiviral. Another method consisted in the use of an insufflator with a bent stem that could be curved round the lower edge of the soft palate, permitting a retrograde insufflation capable of reaching the whole surface of the nasopharyngeal cavity, the posterior nares, the orifices of the Eustachian tubes and the larynx. Following this procedure, the patient was told to expectorate and blow his nose, following which he was given another insufflation in the front of the nose. Of 30 patients, 80 per cent showed improvement and recovery. Only the organisms predominating in the particular infections of the nose and throat should be used in these bacteriologic preparations. Stock strains should not be used, in the opinion of these authors, in the preparation of either antiviral or bacteriophage.

The use of bacteriophage for treating cases with chronic pyelitis is not strikingly successful. While the condition may be somewhat improved, according to H. Christiansen (*Ugeskr f læger* 92 387 (Apr 17) 1930), if the specific bacteriophage that causes rapid and complete lysis of the patient's bacteria is obtained, the results are not uniformly gratifying. Due regard must be paid to the acid reaction of the urine in colurias and it is necessary that the urine be made alkaline before treatment.

E. D. Crutchfield and B. F. Stout (*Arch Dermat and Syph.* (Dec) 1930) set forth the importance of using a phage capable of producing strong transmissible lysis in the treat-

ment of staphylococcic infections of the skin and point out that lack of success is probably often due to a diminution in the lytic power. The importance of a laboratory check to insure uniform results is emphasized. Specific virulence to the offending organism should be tested when possible, and an autogenous phage is desirable if the delay is justifiable.

It was found that a combination of local applications and subcutaneous injection gave the best results, but in very superficial small areas, local applications proved quite efficacious alone.

Fifty-seven cases are reported, including deep seated furuncles, folliculitis of the acne varioliformis type, *sycosis vulgaris*, deep-seated pyoderma, *ecthymatous*-like lesions, acute virulent infections such as cellulitis and carbuncles, and a group of cases of a pustular type of acne. The conditions treated were chronic or acute, and the ages of patients varied from 2 months to 64 years. The number of injections in each case varied from 1 to 31, averaging  $5\frac{1}{3}$ . Dosages of subcutaneous injections varied between 0.25 c.c. and 4 c.c. The standard dosage was 1 c.c. each at 48-hour intervals. In this important group all methods of employing a bacteriophage were used. Most of these cases received injections and many of them local applications as well. Those not injected were treated by local applications. Some local injections were also given.

The results of this treatment are reported as better in these cases than in similar cases in which other means of treatment were used. Such results cannot be expected, however, without a bacteriophage which is known to lyse the infecting organism and capable of transmitting this power.

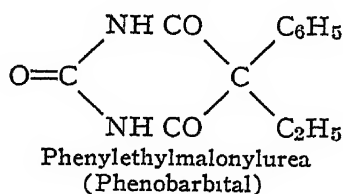
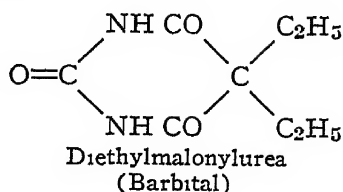
**BARBITAL AND DERIVATIVES.**—Barbital and its various derivatives are by far the most widely used of the newer hypnotics furnished to the medical profession by the pharmaceutical houses, according to G. W. Collins and P. N. Leech (*J. A. M. A.* 96:1869 (May 30) 1931). Next to the barbital group, the sulphone derivatives are the most popular, the hypnotic property of which is said to increase with the number of ethyl groups present. Among the most important of the drugs used for hypnosis are the ureides or compounds of urea, which is an end product of protein metabolism. Urea, which is regarded as an amino compound, may be joined with acids with a resultant loss of water, producing a number of chemical substances analogous to amides. The reaction of urea and malonic acid forms a compound known as malonylurea, another name for which is barbituric acid.

The 2 hydrogen atoms in the methylene or  $\text{CH}_2$  group of malonylurea are very reactive, as pointed out by Collins and Leech. They may be replaced by bromine, hydroxy, nitro- or *iso*-nitroso, furthermore, 1 or 2 ethyl, *iso*-butyl, *iso*-propyl, amyl, allyl or other groups may be substituted, producing varieties of the hypnotic drugs.

The substitution compounds are prepared and advocated by the various pharmaceutical houses which claim special virtues for the individual compound. Under the name of *veronal*, Emil Fischer and von Mering first introduced barbital or diethylbarbituric acid to the medical profession. This still remains one of the most useful hypnotics of all, and certainly the leading hypnotic of the malonylurea series. *Phenobarbital* differs from barbital by a slight chemical modification, one of



the ethyl groups being replaced by a phenol group



Since the sodium salts are freely soluble in water and the acids are but sparingly soluble, numerous sodium preparations have been placed on the market. Collins and Leech have arranged a splendid chart (page 136), which clearly describes the essential chemical groups and the modifying groups contained within the various barbituric acid sedative compounds.

That the use of *phenobarbital* is not invariably a safe procedure is proven by a case exhibiting a skin eruption reported by M. G. Peterman (J A M A 97 703 (Sept 5) 1931). This writer cites the description of A S Jackson (J A M A 88 642 (Feb. 26) 1927) who reviewed the literature and described 6 cases showing an erythematous rash which may involve portions or the skin of the entire body. Fever, gastrointestinal disturbances and cerebral symptoms may be noted. There is likewise an exanthem and a conjunctivitis, and Peterman described a measles-like toxic reaction in a 6 year old child who showed the classical clinical picture of rubeola except for the absence of Koplik spots.

The author describes a case which had been given bromides, the use of which was continued while away from

medical supervision. Numerous scattered papular lesions on the face and lower third of the leg, as well as on the forearm above the wrist, were noted and these were surrounded by smaller lesions. The eruptions consisted of the typical multiple round, reddish, firm, "anthracoid" elevations with rolled edges. When coming under medical supervision again, the bromides were discontinued and phenobarbital was substituted. The lesions gradually disappeared, and in 6 months only the scars were noted. At this time the dosage of phenobarbital was doubled, and a week later, small vesiculopapular lesions were observed on both legs and forearms at the sites of the healing bromoderma granulomas. These lesions increased in size and practically resembled the original bromide eruptions. After this, the author substituted *sodium amytal* for the phenobarbital and the new lesions disappeared within a month. The author states that iodized salt was used on the food throughout the period and may have been a factor in the slow healing.

Since the list of barbituric acid derivatives is growing so rapidly, the danger of *acute poisoning* by these compounds, given either as anesthetics or as hypnotics before anesthesia, becomes more important. Likewise, the laity, as pointed out by A H Maloney, R H. Fitch and A L Tatum (J Pharm and Exper Therap 41:465 (April) 1931), are using these drugs for their hypnotic qualities, without medical supervision, and are adding to the incidence of accidental deaths by promiscuous self-medication. Furthermore, these authors call attention to the employment of various barbituric acid derivatives for suicidal purposes. Because of the increasing importance of the toxic effect

## AS THE CHEMIST SEES BARBITAL COMPOUNDS

	ESSENTIAL GROUP	MODIFYING GROUPS	MELTING POINT
Barbital (USP)-----	$\begin{array}{c} \text{H}-\text{N}-\text{C}=\text{O} \\   \\ \text{O}=\text{C}-\text{N}-\text{H} \end{array}$	$\begin{array}{c} \text{C}_6\text{H}_5 \\   \\ \text{C}_6\text{H}_5 \end{array}$	187-190 C
Phenobarbital (USP)---	$\begin{array}{c} \text{H}-\text{N}-\text{C}=\text{O} \\   \\ \text{O}=\text{C}-\text{N}-\text{H} \end{array}$	$\begin{array}{c} \text{CH}-\text{CH}_2 \\   \quad   \\ \text{CH}=\text{CH} \\   \\ \text{C}_6\text{H}_5 \end{array}$	172-174 C
Allyl iso Propyl Barbituric Acid-----	$\begin{array}{c} \text{H}-\text{N}-\text{C}=\text{O} \\   \\ \text{O}=\text{C}-\text{N}-\text{H} \end{array}$	$\begin{array}{c} \text{CH}_2\text{CH CH}_2 \\   \\ \text{CH}(\text{CH}_3)_2 \end{array}$	138-139.50
<small>The hypnotic in ALLONAL* and ELIXIR ALURATE*</small>			
Amytal-----	$\begin{array}{c} \text{H}-\text{N}-\text{C}=\text{O} \\   \\ \text{O}=\text{C}-\text{N}-\text{H} \end{array}$	$\begin{array}{c} \text{CH}_2\text{CH}_2\text{CH}(\text{CH}_3)_2 \\   \\ \text{C}_6\text{H}_5 \end{array}$	153-155 C
<small>(The mono sodium salt is known as AMYTAL-SODIUM)</small>			
Dial-----	$\begin{array}{c} \text{H}-\text{N}-\text{C}=\text{O} \\   \\ \text{O}=\text{C}-\text{N}-\text{H} \end{array}$	$\begin{array}{c} \text{CH}_2\text{CH CH}_2 \\   \\ \text{CH}_2\text{CH CH}_2 \end{array}$	171-173 C
Ipral-----	$\begin{array}{c} \text{H}-\text{N}-\text{C}=\text{O} \\   \\ \text{O}=\text{C}-\text{N}-\text{H} \end{array}$	$\begin{array}{c} \text{C}_6\text{H}_5 \\   \\ \text{CH}(\text{CH}_3)_2 \end{array}$	200-203 C
<small>(The calcium salt)</small>			
Neonal-----	$\begin{array}{c} \text{H}-\text{N}-\text{C}=\text{O} \\   \\ \text{O}=\text{C}-\text{N}-\text{H} \end{array}$	$\begin{array}{c} \text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2 \\   \\ \text{C}_6\text{H}_5 \end{array}$	124-127 C
Nostal *-----	$\begin{array}{c} \text{H}-\text{N}-\text{C}=\text{O} \\   \\ \text{O}=\text{C}-\text{N}-\text{H} \end{array}$	$\begin{array}{c} \text{CH}(\text{CH}_3)_2 \\   \\ \text{CH}_2\text{CBrCH}_2 \end{array}$	177-179 C
Pentobarbital-----	$\begin{array}{c} \text{H}-\text{N}-\text{C}=\text{O} \\   \\ \text{O}=\text{C}-\text{N}-\text{H} \end{array}$	$\begin{array}{c} \text{C}_6\text{H}_5 \\   \\ \text{CH}(\text{CH}_3)\text{CH}_2\text{CH}_2\text{CH}_2 \end{array}$	128-131 C
Pernoston *-----	$\begin{array}{c} \text{H}-\text{N}-\text{C}=\text{O} \\   \\ \text{O}=\text{C}-\text{N}-\text{H} \end{array}$	$\begin{array}{c} \text{CH}(\text{CH}_3)\text{CH}_2\text{CH}_2 \\   \\ \text{CH}_2\text{CBrCH}_2 \end{array}$	130-132 C
<small>(The mono sodium salt)</small>			
Phanodorn-----	$\begin{array}{c} \text{H}-\text{N}-\text{C}=\text{O} \\   \\ \text{O}=\text{C}-\text{N}-\text{H} \end{array}$	$\begin{array}{c} \text{CH}-\text{CH}_2 \\   \quad   \\ \text{CH}_2-\text{CH}_2 \\   \\ \text{C}_6\text{H}_5 \end{array}$	171-174 C
Proponal *-----	$\begin{array}{c} \text{H}-\text{N}-\text{C}=\text{O} \\   \\ \text{O}=\text{C}-\text{N}-\text{H} \end{array}$	$\begin{array}{c} \text{CH}(\text{CH}_3)_2 \\   \\ \text{CH}(\text{CH}_3)_2 \end{array}$	145 C
Rutonal *-----	$\begin{array}{c} \text{H}-\text{N}-\text{C}=\text{O} \\   \\ \text{O}=\text{C}-\text{N}-\text{H} \end{array}$	$\begin{array}{c} \text{CH}-\text{CH}_2 \\   \quad   \\ \text{CH}=\text{CH} \\   \\ \text{CH}_3 \end{array}$	226-228 C
Sandoptal *-----	$\begin{array}{c} \text{H}-\text{N}-\text{C}=\text{O} \\   \\ \text{O}=\text{C}-\text{N}-\text{H} \end{array}$	$\begin{array}{c} \text{CH}_2\text{CH}(\text{CH}_3)_2 \\   \\ \text{CH}_2\text{CHCH}_2 \end{array}$	138-139 C

The preparations indicated by a star do *not* stand acceptable by the Council on Pharmacy and Chemistry of the American Medical Association for inclusion in New and Non-official Remedies—March 1, 1931. If other than official preparations are desired, physicians who follow the Council should limit their prescriptions to N N R preparations.

of barbiturates, these investigators sought for an effective antidote to be used in cases of poisoning from the barbituric acid compounds.

They cite, in passing, various procedures of an antidotal nature previously advised and describe the work of Caussade and Tardieu who, in 1925, advised blood-letting in the treatment of *barbital poisoning* and of Gower and Tatum who in 1929 advocated the use of moderate continuous diuresis.

Extensive experimentation on dogs and rabbits showed that coramine, strychnine, brucine, cocaine, physostigmine, ephedrine, calcium gluconate and insulin have proven to be inefficient as antidotes to barbiturate poisoning. Picrotoxin, on the other hand, proved effective against *acute poisoning* from the shorter acting barbiturates in rabbits and dogs when amytal, pernocton and nembutal of the barbituric acids were used. Picrotoxin was given by

intravenous, intramuscular, and subcutaneous methods of injection. Because of its margin of safety, Maloney and his co-workers recommend its clinical employment, and suggest that small doses repeated at intervals are more to be desired than 1 or 2 large doses.

### **BASAL GANGLIA, DISEASES OF.—HEPATOLENTICULAR DEGENERATIONS.**

—Of particular interest in diseases of the basal ganglia are the hepatolenticular degenerations. The association of lenticular disease with cirrhosis of the liver has been frequently studied clinically, pathologically and experimentally by many authors. Wilson, in 1912, pointed out that progressive lenticular degeneration, with chronic changes (and acute as well) in the putamen and caudate nuclei, was definitely associated with a nodular hypertrophic cirrhosis of the liver. Since that time other authors have added to the original picture and Wall, in 1921, included Fleischer's pseudosclerosis. This latter condition shows a peculiar greenish-brown corneal pigmentation of Descemet's membrane near the limbus and is called the Kayser-Fleischer zone, which is considered pathognomonic of hepatolenticular degeneration. J Lhermitte and W. S. Muncie (Arch Neurol and Psychiat 23 750 (Apr) 1930) studied 3 cases in one family of cirrhosis of the liver, with the Kayser-Fleischer zone in but one of them. This case showed no marked involvement of the nervous system. The authors believe that such findings make it possible to extend the conception of hepatolenticular degeneration with varying manifestations of the disease. They group the possibilities as follows. (1) Liver, brain and cornea, (2) liver and brain,

(3) liver and cornea, (4) liver alone, (5) brain and cornea, (6) brain alone, (7) cornea alone. In the 3 cases studied there was gastric anacidity which raises the question of a gastrointestinal (toxin) etiological factor.

The essential characteristics of lenticular degeneration (sometimes called the syndrome of Wilson or Wilson's Disease) are hypertonicity of muscles, tremor (of a regular rhythmical character), dysarthria, dysphagia and hypertrophic cirrhosis of the liver.

### **SPASMODIC TORTICOLLIS.**

—Another lenticular disease manifested by hyperkinesis has received considerable attention from the neurosurgeons. This is *spasmodic torticollis* and is viewed by most authors as a partial manifestation of dystonia musculorum deformans or torsion spasm. It is occasionally unilateral, but most often bilateral, and frequently extends from the muscles of the neck to muscles in all other parts of the body. In spasmodic torticollis, G B Hassin (Arch Neurol and Psychiat 26 1043, 1931), points out that the sternomastoid and trapezius muscles stand out prominently and are very firm to palpation. The head movements are jerky and twisting, usually in some particular direction. It was formerly held that torticollis was a functional or psychogenic disorder, but with more extensive investigative work on the basal ganglia, the seat of the disorder has been found to be an actual organic pathologic condition. Hassin discusses the differential aspects of the functional and organic neck movements and states that the functional are *clonic* tic-like movements, while the organic are *tonic*. Functional cases are rare. The *organic cases* are amenable to **surgical treatment**, the accepted procedure being an excision of those spinal nerve roots

which control the motor activity of the muscles involved

**Surgical Treatment.**—W. E. Dandy (Arch. Surg 20 1021 (June) 1930) states that the movements are never restricted to the muscles of one side of the neck and that consequently a unilateral operation is of little value. He performs a high cervical laminectomy and cuts the motor roots of the first 3 cervical nerves bilaterally. Then the spinal accessory nerves are cut peripherally through 2 separate cervical incisions. The patients at first complain that the head feels insecure, but they soon train themselves to use the preserved muscles. In 7 patients under his care, 5 were cured and 2 were improved.

C. E. Dowman (Surg Gynec Obst. 53 836 (Dec) 1931) describes the treatment of spinal contractions of the neck muscles involving the sternocleidomastoid on the right and the posterior neck muscles and left platysma, as well as some of the right posterior neck muscles, by a series of operations. The muscles involved were isolated from their nerve supply. The following procedures are necessary to bring relief: first, section of the spinal accessory branches to the sternocleidomastoid on the right showed a moderate amount of improvement and was followed 8 days later by a laminectomy and the destruction of the second, third and fourth posterior roots on both sides, as well as the first, second and third anterior roots on the left, thus removing the sensory impulses and paralyzing to a large extent the deep posterior muscles on the left side. Following this procedure there was very marked improvement, but the spasmodic contractions of the left platysma and left trapezius muscles remained, producing marked elevation of the left shoulder. Six

months later the third operation was performed and the peripheral branches of the facial nerve to the platysma, as well as the branches of the spinal accessories to the trapezius, were destroyed. A definite improvement resulted in the movements confined to this group. There remained, however, pulling of the deep posterior muscles of the neck, on the right, which had not been isolated from their nerve supply at the second laminectomy. Another laminectomy was, therefore, undertaken and the first, second, third and fourth anterior roots, on the right, were divided, as well as both of the fifth cervical posterior roots. Following this operation there was complete absence of spasmodic movements, and there had been no return of these movements even 18 months after the final operation.

The widespread destruction of the first, second, third and fourth cervical anterior roots on each side, as well as the upper 5 posterior cervical roots showed no untoward complications, as far as the movement of the head was concerned. In fact, the author reported that these movements were apparently normal.

The necessary selection of certain branches of the cervical and spinal accessory nerves is an important consideration and each case of spasmodic torticollis requires an individual analysis to determine the necessary combinations of neurectomies and posterior root sections required. Dowman (*Ibid*) points out that it was not possible to isolate the groups of muscles to be destroyed until after some of the major components had been isolated indicating the remaining offenders.

The various results obtained by Foerster, McKenzie, Cushing and Frazier have been based upon the work of Sher-

rington and Spiller and indicate that it is necessary to destroy the sensory tonic neck reflex stimuli carried through the posterior roots as well as to destroy the motor supply of the muscles themselves. The combination of motor and sensory root destruction reported by Dowman has offered the best solution to this complicated problem so far presented. Mills stoutly maintained throughout his life that the disturbance was of central origin and that little hope could be expected from isolated operative procedures on the periphery. It is evident that only by a massive blocking out of sensory and motor fields to the involved area, can the many factors responsible for the frequent discharge of the uncontrolled central nuclei be controlled.

**PARALYSIS AGITANS OR PARKINSONISM.**—This was studied by M. Keschner and P. Sloane (Arch Neurol and Psychiat 25 1011 (May) 1931), who submitted a report on 7 cases, 3 of which were chronic encephalitic parkinsonism, 2 idiopathic parkinsonism, and 2 arteriosclerotic parkinsonism. From the standpoint of symptomatology the chronic encephalitic cases showed typical mask-like rigidity, sometimes tremors (not usually pill-rolling in type), oculogyric and cephalogyric crises, tic-like movements, myoclonia, greasy skin, respiratory disturbances (hyperpnea and dyspnea), reversal of sleep curve, pyramidal tract involvement, definite mental changes, history of an acute illness with fever, and occurring in younger people than either of the other 2 types.

The characteristics of idiopathic paralysis agitans are totally unlike those of encephalitic parkinsonism, except in the rigidity. This type usually begins in one or another extremity—usually an arm—then involves the lower extremity

of the same side. Later on, the opposite lower extremity is affected and still later, the arm. The head is usually the last to be involved. (In the encephalitic type all areas are affected simultaneously—but may show distinct progression in severity.) Rigidity is sometimes present without tremor, but this is exceptional. Usually there is “pill-rolling” tremor, early development of the mask-like face, and an absence of the other manifestations common to the encephalitic variety. The age of onset is later than in the other group and is usually in the prearteriosclerotic period.

In arteriosclerotic parkinsonism the syndrome of rigidity and tremor may be complete or only partial, occurring definitely in arteriosclerotic persons and later in life than in the other two types. The onset may be abrupt, corresponding to a vascular insult. The progress of the disease is usually rapid, and tremor is not so common, nor is festination and propulsion. The rigidity is uneven and a cog-wheel phenomenon is lacking. Catatonic tendencies are increased as is also the possibility of only one side of the body being affected. Vegetative disorders are minimal or absent and muscle rigidity is more marked in the lower than the upper extremities. Psychic changes of the arteriosclerotic type are common, *vis*, disturbances of memory, irritability, emotional instability and explosive laughter and crying. In short, the characteristics are those of parkinsonism plus other evidences of focal cerebral or cerebellar disease.

*Differential diagnosis* between the 3 types is sometimes difficult, but when the distinctly typical features of the encephalitic type are kept in mind, that group is readily eliminated or substantiated. The mode of onset helps to differentiate the other 2, as well as the

clear mentality of the idiopathic type, in contrast to the psychic deterioration in the arteriosclerotic

**PATHOLOGY.**—Keschner and Sloane (*Ibid*) found considerable confusion in the pathological pictures and were unable to clearly separate the 3 groups. Common to them all were “extensive chronic, diffuse parenchymatous changes involving the pallido-nigral system.” The pallidum (of the lenticular nucleus) was involved in all cases, though more markedly in the idiopathic and arteriosclerotic cases. The putamen (of the lenticular nucleus) was not involved in all cases, nor did the degree of involvement of pallidum and putamen correspond with the clinical symptomatology. The thalamus was involved in all except 1 encephalitic case. Perivascular infiltrations seemed to be a common pathological finding in encephalitic cases and absent in the others. The red nucleus, hypothalamus and corpus luyssii were inconstantly affected.

The cell changes were typical of chronic degenerative processes and the longer the duration of the disease, the more closely all types resembled the idiopathic. From a pathological standpoint the authors concluded that differentiation of the 3 types could not be clearly made.

**BENZENE POISONING.**—Pollution of the air by dust and by motor vehicle exhaust as an etiological factor in the causation of bronchial carcinoma—which has been increasing in recent years—is mentioned by M. Schmidtman (Klin Wchnschr 9:2106 (Nov. 8) 1930). From experiments on several groups of animals, this author found that when small amounts of benzene or benzine were inhaled during long periods, the animals developed emphy-

sema, chronic bronchitis with epithelial proliferations and atelectatic pneumonias. Many of the animals showed extensive epithelial metaplasias in the pulmonary alveoli, however, neither here nor in the proliferating bronchial epithelium could malignant growth be detected. The blood-forming apparatus was injured and gradually there developed the same changes that are noted in experimental benzene poisoning. In the inhalation experiments a leukemic stage was noted. From his experiments, this author concludes that, contrary to expectations, the general changes rather than the local changes in the lungs are of greater significance. Although the quantities of benzene used were small, the pollution of the air in the streets is still less, and therefore, it would be difficult to determine the effect on human beings in such small quantities. However, in enclosed industrial plants in which benzene or similar substances are used, the concentration would be greater than that used in experiments, and harmful effects might easily result.

**TREATMENT.**—A case of acute benzene poisoning occurring in a painter is described by D. S. Pulford (California and West Med 35:36 (Nov) 1931). The patient showed hemorrhage from the gums, with marked anemia and leukopenia. Repeated transfusions were given, to which the patient responded promptly. The case is cited by the author to emphasize the necessity of considering benzene poisoning in the differential diagnosis of conditions accompanied by a marked leukopenia.

While transfusion has been the method of choice in treating cases of severe chronic poisoning from benzene fumes, a case treated by liver diet after 3 transfusions had been ineffective, is



described by A R Smith (J A M A. 93 1970 (Dec 21) 1929) The patient was a Greek-American laborer, aged 38, admitted to the hospital for severe bleeding from the gums of 3 weeks' duration, with frequent epistaxis and spontaneous black and blue spots appearing on the skin during the 2 weeks previous to admission

While employed in an artificial leather shop, he worked in a coating room applying a benzene-rubber compound, which he scooped out of a barrel, to the material to be coated Soon after taking on this work, anorexia and occasional nausea, with vomiting about once a week, were noted Later, an itching of the skin and extremities, and at times bleeding from the gums, was observed

Following a tooth extraction, bleeding from the socket persisted, and 2 weeks before hospital admission the patient suffered from epistaxis which occurred 3 or 4 times, and during this period the sudden appearance of numerous purplish areas over the body was noted Two teeth were extracted, the bleeding from the sockets being profuse The physician gave calcium by mouth and 40 c.c. (10 drams) of a thromboplastic substance hypodermically and packed the socket for relief of bleeding but with no result The case was diagnosed as purpura hemorrhagica and referred to the hospital

On admission the temperature was 101.2° F. (38.4° C); pulse rate, 96, respiration 24, blood-pressure 125 over 80. Halitosis, with the teeth in poor condition and numerous bleeding points in the gums, were noted Blood count showed hemoglobin, 62 per cent; red blood cells 3,300,000, white blood cells, 1350; polymorphonuclears, 25 per cent, lymphocytes, 75 per cent; platelets, 25,000. The bleeding time 33 minutes

Following the history of exposure to benzene, and the marked leukopenia, a diagnosis of chronic benzene poisoning was made and a direct transfusion of 500 c.c. of blood was given the day after admission Following this, oozing ceased, but commenced 4 days later, when the blood count showed hemoglobin 56 per cent; red blood cells, 2,820,000, white blood cells 1300, polymorphonuclears, 36 per cent A second transfusion of 200 c.c. was given by the indirect method, 6 days after the first, and a third of 500 c.c., by the same method, was made 3 days later

With no response from the 3 transfusions, the effect of liver therapy was tried, ½ pound (240 Gm) daily of liver being included in the diet The white cell count was 1480 three days later, showing a slight increase, and it was then, for the first time, greater than it had been on admission Eight days later, the white cell count was 3900, though the hemoglobin remained low, 39 per cent, erythrocytes did not improve Coincidentally with improvement in the leukocyte count, bleeding from the gums diminished and was practically absent several days later Following a month of liver therapy, the reticulocytes reached 86 per cent, whence they gradually diminished to 31 Improvement in the hemoglobin and erythrocytes lagged behind that in the leukocytes Liver therapy was continued for 7 weeks. Cessation of this diet did not bring about a fall in the blood count

At the time of discharge from the hospital, hemoglobin was 59 per cent, erythrocytes 3,780,000, leukocytes 5800, polymorphonuclears, 60 per cent; lymphocytes, 32 per cent; mononuclears, 6 per cent, eosinophiles, 2 per cent; platelets 195,000; and bleeding time 8½ minutes Smith points out that the

chief effects of the liver diet in this case were on the white rather than red cell production. The reticulocyte response, though present, was not similar to that noted in cases of primary anemia.

**BILE FLOW.—PHYSIOLOGY, EXPERIMENTAL.**—C B Puestow (Arch Surg 23 1013 (Dec) 1931) investigated the various factors concerned in the physiology of the flow of bile into the duodenum and devised an operative procedure which permanently exposed to view an isolated portion of the duodenum containing the orifice of the common bile duct. This permitted long and varied observations under different physiologic conditions in animals with minimal anatomic disturbance. By so doing he eliminated the complicating factors of anesthesia and brevity under which previous observations had necessarily been made. He observed that the liver secretes bile continuously (although the amount varies) but that the flow from the common bile duct is intermittent.

The existence of a muscular arrangement at the duodenal end of the common bile duct was accepted by many early workers. Others have felt that no independent sphincter existed and that the constricting force generally attributed to the sphincter of Oddi was due, for the most part, to the tonus of the duodenal musculature. Since it has been shown at numerous times that the resistance offered by the lower end of the choledochus will withstand a pressure equal to that exerted by a column of water 100 to 625 mm in height, the presence of a definite muscular constriction is generally accepted.

Experimentally, the tonus of the sphincter may be decreased by cholecystectomy, by feeding the animal and

by the local application to the duodenal mucosa of acids and certain drugs. The tonus of the sphincter is increased in fasting animals and by the application of alkaline solutions. Puestow notes that Burget, following experiments in which the common bile duct was transplanted into a new site in the duodenal wall, and by other experiments in which the orifice of the duct was cocamized, concluded that the action of the sphincter did not play as large a part as the tonicity and peristaltic activity of the duodenum.

The motor enervation of the biliary tract has been attributed by some to fibers contained in the great splanchnic nerves, others have held vagal fibers responsible. Still another group has held to a theory of contrary enervation which is thought to result in the simultaneous dilatation of the orifice and contraction of the gall-bladder. Respiration, peristalsis, and the ingestion of various foods, especially fat, have been considered to govern, to some extent, the passage of bile into the duodenum.

A constriction at the duodenal orifice of the common bile duct would serve a threefold function: it would regulate the flow of bile into the intestine; prevent the back flow of duodenal contents into the biliary tract; and be a factor in the filling of the gall-bladder.

Puestow devised an operative procedure to bring that segment of the duodenal wall containing the orifice of the common bile duct to the anterior abdominal wall where it could be observed and the flow of bile under varying conditions noted. The technic adopted by Puestow called for a 3-stage operation, carried out aseptically under ether anesthesia. In the first stage the pylorus was divided and the continuity of the gastrointestinal tract

reestablished by uniting the stomach to the jejunum. The animals were allowed to recover. The second stage consisted in the obliteration of the accessory pancreatic duct which opens into the duodenum close to the opening of the choledochus. At this time the duodenum was partially separated from the pancreas, and then brought to lie between the skin and the muscle of the abdominal wall. Finally, in the third stage, the duodenum was divided between the orifice of the common bile duct and the main pancreatic duct. The distal portion containing the opening of the main pancreatic duct was closed. The orifice of the choledochus with the adjacent portion of the duodenum was then brought to the anterior abdominal wall and sutured to surrounding skin. This provided the animal with an isolated segment of duodenum and the orifice of the common bile duct exposed on the abdominal wall.

When the animals had recovered, the flow of bile from the orifice was observed and effects of fasting and the administration of substances orally and subcutaneously were studied. The effect of the local application of certain drugs was also noted. Finally, the gall-bladder was removed and the animals observed under conditions similar to those under which they had previously been studied.

In animals with the gall-bladder intact, it was found that, after a 12-hour fast, bile was not expressed from the orifice, excepting possibly a drop or two following muscular exertion. The orifice was closed for the greater part of the time, although duodenal peristalsis caused dilatation of the orifice proportional to the extent of the activity of the duodenum. There were some exceptions and the orifice was sometimes

open when the duodenum was quiescent (This would suggest a sphincter in the wall of the choledochus proximal to the duodenum). While the animal was fasting, very little activity was noted in the exposed part of the duodenum. The mucosa was pallid and there was a minimum of duodenal secretion. The pressure within the common duct during the fasting period was equivalent to a column of bile 140 to 170 mm high.

On feeding it was found that an initial flow of dark viscid bile followed the sight, smell, or ingestion of the food, and lasted 1 to 4 minutes. This was followed in from 10 to 20 minutes by a second flow, profuse at first, but gradually diminishing, until 3 or 4 hours later it ceased. The orifice, after feeding, was observed to be open, especially when the duodenum was most active. Normal results were obtained when egg yolk and cream were fed to the animal. When lean horse meat was fed, the bile was lighter in color and the flow lasted longer than when the meal consisted of fat alone. The response to different types of foods appeared the same. Water caused an increase of duodenal peristalsis but did not cause a flow of bile. Magnesium sulphate administered by mouth caused vigorous peristalsis but no expression of bile, although a fatty meal shortly afterward was followed by a flow of brown viscid bile. Excitement apparently had an inhibiting effect on the flow of bile. Following feeding, no noticeable changes occurred in the duodenum for from 10 to 20 minutes, then it slowly became hyperemic, and its tonus and activity markedly increased. Duodenal peristalsis reached a maximum in about  $\frac{1}{2}$  hour.

Definite changes in the expression of bile occurred following cholecystectomy.

In the fasting animal there was a constant flow of light colored and watery bile, the rate of flow being modified by the respirations, muscular contractions, and duodenal activity, the latter being negligible in the fasting animal. Feeding produced no changes in the flow of bile. However, the changes produced in the duodenum were found similar to those occurring in animals with the gall-bladder intact. Intraductal pressure was greatly reduced after cholecystectomy and was determined to be equivalent to 20 to 30 mm of bile. The mucosa of the exposed duodenum was treated with various solutions with different findings. Distilled water and dilute alkaline solutions had practically no effect. Physiologic saline excited some duodenal activity but no expression of bile; 25 per cent. magnesium sulphate acted similarly, but caused more marked duodenal activity and an occasional spurt of bile. Dilute hydrochloric acid was most effective in causing duodenal peristalsis and spurts of bile. Bile salts, administered intravenously, was followed in  $\frac{1}{2}$  hour by a profuse flow of light colored, watery bile.

It is difficult to determine the extent of the disturbance to the secretion of bile caused by the unavoidable anatomic derangements in these experiments. At various times during the experiments spurts of bile occurred without any apparent cause. These might have been initiated by a gall-bladder contraction. The fact that cholecystectomy was followed by a low intraductal pressure and a patent orifice suggests a loss of tonus of reflex origin.

**BILIARY TRACT.—CHOLECYSTITIS AND CHOLELITHIASIS.**—Modern methods of investiga-

tion have greatly stimulated interest in diseases of the biliary tract. The contributions to be presented are taken from rather voluminous recent literature and show interesting trends of investigation as well as valuable clinical observations. Inasmuch as cholecystitis and cholelithiasis are closely related etiologically and present similar problems of diagnosis, they will be considered together.

**ETIOLOGY.**—1 *Infection.*—B. Williams and D. G. S. McLachlan (Lancet 2 342 (Aug 15) 1930) studied 106 cases of acute and chronic cholecystitis from the bacteriologic standpoint. They found streptococci in the cystic lymph gland or in the gall-bladder wall in 16 per cent. and *Bacillus coli* in these 2 locations in 20 per cent. at operation. In about 83 per cent. of cases showing streptococci in the cystic gland or gall-bladder wall, the organism was also obtained from the bile. In only 1 instance was a streptococcus isolated from the bile in the absence of stones.

The figures of A. C. Nickel and E. S. Judd (Surg. Gynec. Obst. 50. 655 (Apr) 1930) show an incidence of 50 per cent. positive cultures in 300 surgically removed gall-bladders. No mention is made of bile cultures. Positive cultures were obtained in 68 per cent. of clinically typical acute cases; 51 per cent. in typical chronic cases; 35 per cent. in vague or atypical cases, and 50 per cent. in stone cases. Streptococci predominated in 44 per cent. of the positive cultures, with Gram-negative bacilli and staphylococci predominating in 30 and 26 per cent. respectively. Gall-bladder lesions were produced in 30 per cent. of 132 rabbits injected with cultures of the organisms obtained. It is concluded that streptococci, and occasionally colon bacilli, obtained from

grossly diseased gall-bladders are of etiologic significance since they tend to reproduce cholecystitis in rabbits when injected intravenously

The rôle of infection in the formation of gall-stones was studied by D. M. B. Gross (J. Path. and Bact. 32: 503 (July) 1929). He analyzed 802 cases of gall-stones found in a series of 9531 autopsies. In non-stone cases used as controls the incidence of cholecystitis was 4.1 per cent. Grouping all types of stone cases together, cholecystitis was found, pathologically, in 17.5 per cent. The highest incidence, 21.8 per cent, was found associated with "facetted" stones, while 14.3 per cent of cases with "pigment" stones showed evidence of cholecystitis. Grouping facetted and pigment stones together, the incidence of cholecystitis was 36.1 per cent, as compared with 3.2 per cent inflammation found with single cholesterol stones. It is assumed that infection was associated with the inflammatory changes in most cases. The importance of infection and inflammation in the production of certain types of stones is suggested by Gross' statistics.

E. Andrews, Schoenheimer and L. Hrdina (Proc. Soc. Exper. Biol. and Med. 28: 944, 1930) state that cholesterol is held in solution in human bile by bile salts. Any condition resulting in absorption of bile salts by the gall-bladder results in precipitation of cholesterol. Normally, if absorbed at all, these substances are removed proportionally. After inducing inflammatory change in the gall-bladder of dogs it was found that cholesterol concentration increases, while bile salt concentration decreases. The ratio of bile salts to cholesterol in normals varied from 10-24 to 1. In 9 stone cases in which the bile was analyzed immediately post-

operatively, the ratio averaged 3.4 to 1, and in mixed bile of 30 stone cases averaged 0.6 to 1. Two normal cases analyzed by Hammarstein (cited by Andrews *et al.*) showed ratios of 10 to 1 and 40 to 1, respectively.

These findings indicate that cholesterol is precipitated in the presence of infection, although there is no statement as to the type of stones present in the gall-bladders studied. That such a mechanism cannot explain the formation of all gall-stones is suggested by the lack of inflammatory change in the cholesterol types as reported by Gross, and the common finding of asymptomatic cholesterol stones, in otherwise fairly normal gall-bladders, at operation or autopsy.

**2 Metabolism.**—(a) *Pregnancy*.—The literature contains inferences that the formation of gall-stones is often associated with pregnancy. It has been suggested that the hypercholesterinemia usually present in the pregnant woman is responsible. Gross's (*loc cit.*) statistics fail to support this view. In his series 89.8 per cent of women with stones were married, while 86.6 per cent of women without stones were married. Stones were found in 21.5 per cent of single women and in 27.5 per cent of married women. In analyzing the cases having solitary cholesterol stones it was found that the incidence in females was 4.6 per cent as against 2.1 per cent in males. Three and nine-tenths per cent of single women had this type of stones, 5.4 per cent. of married women, and 2.1 per cent of men, showing a slight increase in the incidence of cholesterol stones in married women. The exact data concerning pregnancy, however, are not given.

(b) *Diabetes*.—That the disturbed cholesterol metabolism so frequently found in diabetes may be related to the

rather frequent occurrence of gall-stones in this disease is suggested by Gross's (*loc cit*) figures. The incidence of all types of stones in diabetics was 25.7 per cent as compared to 15.6 per cent in the controls. Single cholesterol stones were found in 11 per cent in the diabetic series as compared to 2.5 per cent in the controls.

(c) *Obesity*—Gross (*loc cit*) observed a definite relationship between obesity and gall-stones and found that the group with stone averaged being 20 per cent heavier than the group without stones.

It is of interest to note that 97 per cent of the gall-bladders containing cholesterol stones were grossly normal and that in 92 per cent of the cases of this type of stone the finding was accidental, no clinical diagnosis having been made.

3 *Biliary Stasis*.—According to E. L. Walsh and A. C. Ivy (Ann Int Med 4:134 (Aug) 1930), the most accepted theory of the origin of gall-stones is bile stasis. Beyond this, views vary greatly. Naunyn believed ascending infection resulted in stone-forming catarrh; he did not attach great significance to diet nor to cholesterol metabolism. Aschoff and Bacmeister classify gall-stones into noninflammatory, or metabolic, and inflammatory stones. They believe that the cholesterol stone is due to increased cholesterol content of the bile plus concentration and stasis in the gall-bladder. Halpert has suggested that failure of the diseased gall-bladder to absorb cholesterol results in stone formation.

Hoping to gain information regarding the etiology of gall-stones in man, Walsh and Ivy repeated experiments showing that human gall-stones of the mixed type were absorbed in the gall-bladder of the

dog. It was found that the stone began to lose weight within 3 days and in the course of 65 to 156 days would lose from 20 to 96 per cent of its weight. However, if chronic fibrous cholecystitis developed, the stone lost only little weight. Coconut and olive oils added to the diet did not alter the rate of absorption. Induction of biliary stasis by ligation of the cystic duct, stricture of the common duct, or reversal of duodenal peristalsis led to decreased absorption of the stone and an associated inflammatory condition of the gall-bladder wall and precipitation of flakes of pigment and carbonates. *In vitro* experiments showed that there is a marked difference between the cholesterol-saponifiable ratio in human bile and dog bile, which these authors believe is the cause of absorption of human stones when placed in the gall-bladder of a dog. Walsh and Ivy believe that further studies along similar lines may reveal methods of decreasing the incidence of gall-stones.

**INCIDENCE AND DIAGNOSIS**—In W. C. Alvarez's cases (Ann Int Med 4:39 (July) 1930) 44 per cent of the patients with organic gastrointestinal disease had gall-bladder pathology as the chief finding. Gross found gall-stones in 84 per cent. of 9531 autopsies.

Of the various diagnostic procedures introduced for the study of gall-bladder disease, *cholecystography* has received most attention. The value of this examination cannot be denied, but it is not infallible. In gall-stone cases, B. P. Kirklín (Collected Papers of Mayo Clinic 20:91, 1928) found positive evidence of stone in 40 per cent. by the oral method, and J. T. Case (J. A. M. A 92:291 (Jan 26) 1929) 53 per cent by the intravenous technic. Bockus,



Shay, Willard and Pessel (J A M A 96 311 (Jan 31) 1931) reported 96 cases of gall-stone disease in which a positive diagnosis of stone was made by cholecystography in only 29.2 per cent. However, in 88.4 per cent evidence of a pathological gall-bladder was found by this method. Normal gall-bladder shadows were found in 11.6 per cent of this series of stone cases.

S. Moore (J A M A 95 1957 (Dec 29) 1930) has reviewed the experience of 6½ years with cholecystography. The preferable dye is phentiothalein sodium (N. N. R. (phenol-tetraiodophthalein sodium)), according to this author. Intravenous administration is the most reliable method in suspected gall-bladder cases, oral administration only being used by the writer in vague cases where the symptoms do not warrant the intravenous procedure. Of 1290 cases reported, reactions occurred in 34 per cent, 19.7 per cent were mild, and 14.3 per cent severe. By mild reactions are meant any subjective symptoms whatsoever; severe reactions included chills, urticaria, giddiness or malaise. More severe reactions, such as a fall in blood-pressure or fainting were not encountered.

The results of 406 operated cases showed the following:

	Cases	Per Cent Check at Operation
1 Deficiency of concentration	167	98.2
2. Nonvisualization	146	100.0
3 Pericholecystitis	23	95.0
4 Calcified gall-stones	40	100.0
5 Noncalcified stones	19	100.0
6 Questionable stones	11	90.0
	<hr/> 406	<hr/> 98.77

Ten cases reported normal by cholecystography were found to be pathological at operation. Only 58 per cent. of 220 operated stone cases were so diag-

nosed preoperatively. These latter figures indicate the danger of relying entirely upon cholecystographic evidence.

The importance of flat plates of the abdomen in the diagnosis of gall-bladder disease has been emphasized by N. W. Jones, D. L. Palmer and R. B. Adams (Am J M Sc 180 531 (Oct) 1930). Studies are reported on 4820 patients. A diagnosis of cholecystitis was made 1332 times, 459 were operated on for gall-bladder disease. The methods used consisted of flat plates of the gall-bladder area with special care to avoid confusing gas shadows, stomach and duodenal studies with the barium meal, and in some instances cholecystography, either oral or intravenous.

Direct evidence of gall-bladder disease by this method consisted of a positive gall-bladder shadow without dye and an absent or abnormal shadow with dye. Indirect evidence consisted of gastric motor disturbances or deformity of the pyloric antrum or duodenum. In the 459 operative cases direct evidence appeared as follows: Faint shadow 26.8 per cent, moderate shadow 40.3 per cent, marked shadow 23.7 per cent; no shadow 9.2 per cent. Indirect evidence consisted of motor disturbances in 95.45 per cent and deformities of stomach or duodenum in 35.4 per cent. Stones were visualized in 60.6 per cent of cases found to have stones at operation. A correlation of clinical and operative findings showed 23 cases giving positive x-ray signs but negative operative findings, while 4 cases were negative by x-rays and positive at operation. Chemical analysis of the calcium content of gall-bladder walls removed at operation in 24 cases revealed that the amount of calcium was directly proportional to the degree of shadow produced on the film.

**Biliary Drainage.**—H L Bockus, H Shay, J H Willard and J F Pessel (J A M A 96 311 (Jan 31) 1931) compared biliary drainage with cholecystography in the diagnosis of gall-stones. The diagnosis of stones by this procedure is based upon the finding of so-called calcium bilirubin pigment or cholesterol crystals, or both, in the bile, obtained by the method of Lyon. Either or both of these elements were found in 124 operative cases. Of 18 cases showing only cholesterol crystals, stones were found in 89 per cent. In 34 cases with pigment alone, stones were present in 90 per cent. In the absence of jaundice, calcium bilirubin pigment was found to be 97 per cent accurate in the positive diagnosis of gall-stones. Both elements were present in 72 cases, in all of which stones were demonstrated at operation.

The total series reported by these writers consisted of 148 proved gall-stone cases. A positive stone diagnosis was suggested by drainage in 83.2 per cent and by cholecystography in 29.2 per cent. If evidence of gall-bladder dysfunction by cholecystography is accepted as evidence of gall-bladder disease, then 88 per cent of the cases showed this evidence of pathology as compared with 98 per cent evidence of pathology by drainage.

It is emphasized that repeated examination may be necessary in some cases before a diagnosis can be made. The greatest value of biliary drainage is in those cases giving absent shadows by the cholecystographic technic. In the presence of stone, if gall-bladder bile can be obtained, either crystals or pigment, or both, are usually present. The authors found only 3 cases in the entire series when gall-bladder bile was obtained without the finding of these elements. A normal cholecystogram was present in

11.6 per cent. If only 1 examination can be carried out, intravenous cholecystography offers the best chance of revealing valuable evidence, according to these observers.

The case records of 879 patients operated upon with a preoperative diagnosis of cholecystitis or cholelithiasis were reviewed by A B Rivers and H R Hartman (Arch Int Med 45:523 (Apr) 1930). In all cases the gall-bladder proved to be diseased but a large proportion had additional abdominal disease. Of the group diagnosed cholecystitis (287 cases), 71 per cent. had concomitant lesions, 31 per cent showed chronic appendicitis, 18.9 per cent had some degree of hepatitis; 9.2 per cent. revealed gall-stones; and 6.3 per cent showed evidence of pancreatitis. Of 592 cases diagnosed as cholelithiasis, all had diseased gall-bladders, 84.8 per cent. had stones. Appendicitis was found in 28.9 per cent and 12.7 per cent showed hepatitis and 7.8 per cent pancreatitis.

Of the total group, 58 per cent. showed additional pathology; 29.5 per cent had appendiceal pathology; 14.7 per cent showed evidence of hepatitis; in 7.4 per cent pancreatic involvement was found; and cholangitis appeared in 0.7 per cent. Stones were found at operation in 12.1 per cent. of cases preoperatively diagnosed cholecystitis only, and no stones were found in 15 per cent of those having a preoperative diagnosis of cholelithiasis.

**BILIARY TRACT, SURGERY OF.—OPERATIVE INDICATIONS.**—According to R. P. Rowlands (Brit M. J 1:184 (Feb. 1) 1930) operation for cholecystitis and gall-stones should be carried out before the disease has spread beyond the gall-bladder and cystic duct, so that the dis-

case can be eradicated by cholecystectomy at comparatively small risk. In later cases, drainage of the gall-bladder or common bile duct may have to be established in order to save life. These delayed operations have a much higher mortality and are more often followed by recurrence of symptoms, often demanding secondary operation.

J Favre (Presse méd 38 1282 (Sept 20) 1930) states that the absolute indications for cholecystectomy are (1) Nonfunction of the gall-bladder due to obstruction or to sclerosis and atrophy of the gall-bladder wall, (2) gall-bladder disease in a patient with a family history of cancer or signs indicating malignant change in the gall-bladder, (3) gall-bladder infection, and (4) persistent fistula or recurrence of gall-stones after cholecystectomy.

The indications for cholecystectomy which may be considered absolute are (1) Cholelithiasis in a patient whose general condition necessitates restriction of operative procedures to the minimum; (2) cholecystitis with cholangitis demanding drainage, (3) cholecystitis with biliary obstruction, and (4) a gall-bladder which is inaccessible because of its depth or the presence of dense adhesions.

The author's statistics on the 2 operations run almost exactly parallel as regards the immediate mortality and late results.

Favre emphasizes the importance of supplementing surgical intervention with thorough medical treatment.

**Acute Cholecystitis.**—H. F. Graham (Ann. Surg. 93 1152 (June) 1931) compared the results obtained in 20 cases of acute cholecystitis which were operated upon within 24 hours after the onset of the acute symptoms and 178 cases in which operation was

delayed until the acute symptoms had subsided. In the latter group the mortality was higher, the operations were more difficult, and postoperative complications were more frequent and severe than in the former group.

According to R. H. Miller (*Ibid* 92:644 (Oct) 1930), when acute infection of the gall-bladder is treated conservatively there are 3 possibilities: (1) subsidence of the infection, (2) perforation with the formation of a local abscess, and (3) perforation with the development of general peritonitis. Miller questions whether ability to predict the outcome is sufficient to warrant delay of operation.

The records of 200 consecutive cases which were operated upon for acute cholecystitis state definitely that stones were present in 160. In the records of 40 cases (20 per cent) no mention of the presence or absence of stones is made. Miller believes that there were not even as many as 40 cases without stones, that in some of the records in which stones were not mentioned the surgeon merely neglected to record them. In the records of 19 (9.5 per cent) the presence or absence of adhesions is not stated. The fact that there was no walling off in from one-quarter to one-half of the cases, contrary to a rather common belief, shows the danger of spreading infection in case of perforation.

Twenty-seven (13.5 per cent) of the patients died. In the fatal cases the average length of time from the onset of the condition to the operation was 15 days, whereas in the cases with recovery it was  $8\frac{3}{10}$  days. Of the fatal cases, local perforation occurred in 8, but general peritonitis occurred in none. Cholecystectomy was done in 14 of the fatal cases, and cholecystostomy in 13. Of

the patients who recovered, 75 per cent were treated by cholecystectomy

The author concludes that in the cases of patients who are in poor condition but whose symptoms are not very acute, operation may be delayed for 12 hours to allow for preoperative preparation, but that in cases with persistent fever, tenderness and spasm, and especially cases with severe pain which is not easily controlled, it should be undertaken without delay

**BACTERIOLOGY AND PATHOLOGY OF RESECTED GALL-BLADDERS.**—W H Schultze (Virchow's Arch f path Anat 275 717, 1930) made a bacteriological study of 418 operatively removed gall-bladders, 84.2 per cent of which were obtained from women. More than half of the women were between 20 and 39 years of age. In 27 of the 418 cases neither gall-stones nor histological changes in the wall of the gall-bladder were found and the bacteriological examination was negative

Of the 391 remaining cases, in which cholelithiasis or cholecystitis was present, bacteria were found in 131 (33.5 per cent). Of 110 cases in which the gall-bladder presented acute inflammatory changes, bacteria were found in 89 (81 per cent), and of 281 cases in which the gall-bladder showed chronic changes, bacteria were found in 42 (14.6 per cent)

In more than 50 per cent of the cases with bacteria the colon bacillus was present. This bacillus was found even in gall-bladders with slight changes. Next in frequency were streptococci. These were usually of the green-producing, nonhemolytic variety. Staphylococci, which were much less common, occurred with about equal frequency in the acute and chronic cases

It is evident, therefore, that ascending enterogenous infection of the gall-bladder is much more important than descending hematogenous infection. The frequent discovery of staphylococci by other investigators is ascribed by the author to accidental contamination of the cultures

In the development of cholelithiasis, stasis of the gall-bladder contents and metabolic disturbances are important in addition to infection. This is evident from the greater frequency of the condition in the female

There are also cases of severe gall-bladder necrosis characterized by freedom from bacteria and the occurrence of hemorrhages with or without gall-stone formation. For lack of another explanation, the author assumes that these are due to disturbances such as are associated with acute pancreatic necrosis, but he is unable to offer any definite proof in support of this assumption

In 16 of the 50 cases analyzed by G G Gordon-Taylor and L E H. Whitby (Brit J. Surg 18 78 (July) 1930) the fluid contents of the gall-bladder were infected. The organisms present were *B. coli*, 6 cases, streptococci, 4 cases, *B. welchii*, 3 cases, and other bacteria in 3 cases. The wall of the gall-bladder was infected in 41 cases by the same organism. Intestinal bacteria are the most frequent organisms in gall-bladder infections. *B. welchii* is usually, but not invariably, associated with the acute form of cholecystitis. *B. welchii* is more commonly found in gall-bladder infections and in gall-stones than has hitherto been believed; in nearly 9 per cent. of a series of gall-bladders removed by operation was this organism found. *B. welchii* was found in the center of 13 per cent. of gall-

stones obtained from the postmortem room

Seventy-five gall-bladders removed surgically were studied by W. A. Mackey (Glasgow, M J 115 225 (May) 1931), both pathologically and bacteriologically, in an attempt to trace the process of stone formation. The bacteria found most frequently were nonhemolytic streptococci and coliform bacilli, but in about half of the definitely pathological gall-bladders no organisms could be discovered. Cholecystitis pursues a course of exacerbations and remissions, and it was noted that bacteria were usually absent during the latter periods.

The author believes that cholesterol stones are due to metabolic disturbances rather than infection, and that the presence of stones predisposes to attacks of acute cholecystitis.

**TECHNIC.—Cholecystostomy and Cholecystectomy.**—J. H. Gibbon (*Ibid* 90 367 (Sept.) 1929) has written that cholecystostomy is often a life-saving procedure when other operations upon the biliary tract would carry too great a risk. This is true especially in acute empyema of the gall-bladder and in the cases of patients who are old or in poor general condition, also when the operator is inexperienced.

Stones probably seldom re-form after cholecystostomy. Those found in secondary operations are usually stones left behind at the first operation.

Cholecystectomy represents the ideal operation, yet the author reports that it was possible in only about 70 per cent of 300 operations on the gall-bladder and ducts. It is not without risk, because of the disturbances of the biliary circulation that follow. The danger of injury to the common duct in the application of the forceps to the cystic duct

or to control bleeding from the cystic artery must be borne in mind. It cannot be said that fewer and less crippling adhesions follow cholecystectomy than cholecystostomy. The number and type of adhesions following either operation are dependent upon the type and severity of the infection.

The author has abandoned closure of the abdominal wall without a soft rubber drain, since it is well known that in a small percentage of cases bile leakage occurs after cholecystectomy, either from loosening of the ligature on the cystic duct or from open radicals in the gall-bladder bed.

A dilated common duct in the presence of a functioning gall-bladder means obstruction and should be opened. It is often better to remove the stone through a transduodenal incision than by passing probes or forceps into the common duct, as rough instrumentation is apt to produce injury with subsequent stricture.

W. H. H. Croudace (Brit M J 1 707 (Apr 25) 1931) has reported a case of double gall-bladder discovered at operation and surgically removed with recovery.

The first gall-bladder was of about average size, it contained normal bile and no gall-stones. The second gall-bladder was half the size of the other, the bile being much paler, and it contained 29 small gall-stones. Each gall-bladder had a separate cystic duct.

According to A. Austoni (Clin chir 6 630 (June) 1930), the surgery of the biliary tract is gradually becoming more important because of better diagnostic methods. In this field, unlike most others, postoperative *drainage* is regarded by many as indispensable. However, Haberer concluded that the truly ideal cholecystectomy is subserous

removal of the gall-bladder in which the operative field is covered with peritoneum and the abdomen closed without drainage.

The author reports a series of 215 cases of biliary tract surgery in 110 of which the so-called ideal cholecystectomy was done. These included many complicated as well as simple cases. The best time for the operation is during an afebrile period. Absence of jaundice is most desirable, but the surgeon should not wait longer than from 15 to 20 days for the disappearance of this condition. The gall-bladder may be removed even in the presence of such complications as empyema, pericholecystitis, adhesions, and fistulae. The cystic duct should be doubly ligated, the operative field covered as well as possible with peritoneum, and the abdomen closed without drainage even when hemostasis or peritonization is not complete or there is slight soiling with pus. Austoni's results show that in cases treated by ideal cholecystectomy the mortality is generally lower and the postoperative complications fewer than in those treated by cholecystectomy with drainage.

The principal *complications of drainage* are delayed healing, infection in the abdominal wall, secondary infection with thrombosis in the operative field, unfavorable effects on the heart and circulation, interference with abdominal function, and limitation of the excursions of the diaphragm which predispose to postoperative pneumonia.

The *indications for drainage* include the impossibility of isolating and ligating the cystic duct, insecure ligation of the cystic duct, questionable viability of the common duct, sepsis in the intrahepatic and extrahepatic bile passages, and injuries due to faulty technic.

Various authors discuss cholecystectomy with *drainage* and without drainage. G. Cotte and H. Roland (Rev. de cir. 10:38 (Jan.) 1931) do not drain when an ideal cholecystectomy can be done, and mention some disadvantages of drains. R. S. Fowler (Am. Surg. 93:745 (Mar.) 1931) omitted drainage in 240 cases in which cholecystectomy was done. He concludes that wound infection was as common with drainage as without drainage. After reviewing his cases, the author feels that it is wiser to drain than not to drain.

L. R. Whitaker (Am. J. Surg. 13:273 (Aug.) 1931), in a preliminary report, describes a method of *subperitoneal* cholecystectomy. The method described uses the principle of subserous resection through an opening in the abdominal wall just large enough to deliver the fundus of the gall-bladder.

The indications for the author's technic are (1) a nonsclerotic, non-adherent vesicle from which the serosa will strip readily, and (2) limitation of the disease to the gall-bladder, these conditions being determined by history, laboratory tests, cholecystography, and gastrointestinal x-ray examination.

The disadvantages of the method are a longer operating time, and the necessity for expert dissection and handling of tissues.

The advantages of the method are: smaller abdominal incision, with a minimum of reaction and discomfort about the wound and drainage to the abdominal wall, diminished shock and trauma to viscera, with lessened postoperative distress, more rapid convalescence, fewer adhesions, and a reduction of operative risk.

W. L. Estes, Jr. (Arch. Surg. 23:119 (July) 1931) describes a method of *partial* cholecystectomy and its indica-



tions The author believes that partial cholecystectomy has, and should have, a restricted field. In patients in whom the surgical risk is thought to be great, it should not replace cholecystostomy. Evidence of recurrent disease in the biliary tract has appeared in but 1 of 7 cases, and in none of the cases in which a stone was impacted in the cystic duct. If argument were justified, based on so few cases, it would seem that this operation tends to act as a cholecystectomy—it prevents reformation or regeneration of the gall-bladder and yet permits drainage as in cholecystostomy. It might, therefore, have a field of usefulness also in the rare type of secondary operation on the gall-bladder in which, owing to adhesions or to a liver that cannot be rotated, cholecystectomy, although indicated, would be impossible.

**Cholecystogastrostomy and Cholecystenterostomy.**—On the basis of their personal experience in many patients, L. Bérard and P. Mallet-Guy (Lyon chir. 27.5 (Jan-Feb) 1930) state that cholecystogastrostomy does not invariably result in drainage of the gall-bladder. Bile can at times be excreted intermittently and often obliteration of the duct ensues. The authors do not favor this operation as a means for obtaining without fail modification of the gastric contents. Cholecystogastrostomy, however, does insure internal deviation of the flow of bile and is indicated in *icterus due to retention*. The most frequent indication is given in *cancer of the pancreas*, but the operation is also indicated in patients having *tumors of the bile ducts*. In *chronic pancreatitis* of undetermined origin, and likewise in *stasis of the gall-bladder*, the operation of choice is cholecystogastrostomy. The operation is not advised in stricture of the bile ducts, in patients

with tuberculous lymph nodes of the omentum or in idiopathic dilatation of the bile duct in children. In chronic cholecystitis without lithiasis, and as a rule in infections of the gall-bladder, cholecystogastrostomy is contraindicated. The "legitimate" indication for the operation is determined by a mechanical obstruction of the bile duct, it is not solely a means for obtaining deviation of the bile.

R. H. O. B. Robinson (Lancet, 1 673 (Mar 29) 1930) concludes from his own results that in cases of bile-duct stricture, cholangitis, and induration of the head of the pancreas in which the cystic duct is patent and the gall-bladder is comparatively little changed except for the presence of calculi, cholecystogastrostomy or cholecystoduodenostomy should prove to be the operation of choice. Although some authorities have invariably noted evidence of infection after they have performed these operations on animals, Robinson has performed them both in clinical cases and on animals without producing infection. However, because of the conflict of opinion regarding the risk and degree of ascending infection, he believes that further evidence is necessary before they can be regarded as alternatives to cholecystectomy in the type of case under discussion.

Gatewood and Lawton (Surg Gynec Obst 50 40 (Jan) 1930) state that the results of their series of experiments show again that infection of the gall-bladder, liver and bile tracts follows cholecystogastrostomy in dogs. In this series, as contrasted to their previous series in which the common ducts were ligated and divided, there is no dilation of the common ducts and no evidence of gross food particles, or roundworms in the lumina. Infection is definitely less

when the common duct is not ligated and divided. Such experimental differences suggest the following possible explanations for the differences between laboratory and clinical findings. From their previous experiments and from the work of Lehman, the authors have been led to believe that the stoma of a cholecystogastrostomy would close in the absence of common duct obstruction. While in their present series the stomata remained patent, the tendency undoubtedly is for contraction. The gastric rugæ acted almost like valves and probably partially protected the gall-bladder from extraneous material. Many animals which were apparently healthy when sacrificed, showed very definite bacteriologic and microscopic evidence of hepatic infection. May there not be silent hepatitis in many of the patients who are clinically well? More autopsy data will probably settle this question. Finally, may it not be possible that the human liver is better able to conquer biliary infection than that of the dog? It is a well-known fact that fat metabolism differs materially in the two.

**Reconstruction of the Common Bile Duct and Bile Passages.**—According to E. Horgan (Ann. Surg. 93: 1162 (June) 1931), the disadvantages encountered in the use of the ordinary rubber catheter, the rubber T-tube, and the buried drainage tube in drainage and reconstructive operations upon the common and hepatic ducts, led him to devise an L-shaped rubber catheter. This L-shaped rubber drainage tube was used in 3 cases (Ann. Surg. 1162 1166 (June) 1931).

The advantages of this tube as outlined by the author are that it lends itself to secure and firm anchorage in the bile duct, it is easily removed at the time desired without damaging the anastomo-

sis and supplies adequate means of internal and external drainage of bile.

LeG. Guerry (Ann. Surg. 92: 663 (Oct.) 1930) states that when surgical reconstruction of the bile passages is necessary, direct anastomosis between the bile passages and the duodenum gives the best results. Most failures of autoplasmic reconstructions are due to contraction of the transplanted tissue. Contractions will occur in the absence of a proper submucosa even when the structure transplanted has an epithelial lining. Direct anastomosis assures an ample mucous lining to the reconstructed duct and sufficient submucosa and peritoneal surface to prevent contraction.

To 7 cases which he previously reported, the author adds 2 more in which direct anastomosis was done. In the 4 cases in which it was possible to unite the hepatic duct to the duodenum directly, there was no mortality and a thoroughly satisfactory symptomatic cure was obtained.

L. Jacques (Surg. Gynec. Obst. 52: 1151 (June) 1931) states that the exposure of injured bile ducts is frequently more difficult than their plastic repair. Indigo carmine, injected in adequate amounts intravenously, is excreted in the bile, stains it bluish green, and may aid in guiding the way to the proximal stump. A similar procedure may be of value in detecting leakages of bile before closure of the abdomen following cholecystectomy and common duct operations.

**POSTOPERATIVE COMPLICATIONS.**—Among numerous minor accidents of cholecystectomy, L. van der Elst and M. de Langre (Presse méd. 39: 418 (Mar. 21) 1931) recognize as the most important hemorrhages, bile flow, icterus and postoperative stenoses. The authors point out the high import-

ance of early recognition of the source of a *hemorrhage*, on account of the great differences in its significance (mostly from the bed of the liver or the cystic artery) The former is seldom profuse and in general it stops spontaneously in a short time, while bleeding from the cystic artery is at times grave In arresting the so-called late hemorrhages of cholecystectomy the only difficulty is the already formed adhesions, which make the reintervention much more complicated The authors highly advocate thorough preoperative blood tests (coagulation time test and others)

Postoperative bile flow is generally benign If profuse, it is due in the majority of the cases to a slipping off of the ligature from the cystic duct and exceptionally comes from the common bile duct Usually it stops spontaneously Early postoperative *icterus* is always transitory If it persists, the surgeon must decide whether it is produced by liver deficiency, is just a minor accident of compression, or provoked by an injury to the common bile duct during the operation In many instances it is produced not only by the causes mentioned, but at times also by a stone left in the common bile duct A slight icteric tint may appear on the next day after operation. In a day or two it becomes more marked The authors suggest that the drain be replaced or slightly pulled out, whereupon this symptom will quickly disappear with its accompanying malaise Icterus provoked by the abscess formation at the operative zone and the simultaneous opening of the wound in the abdominal wall, or icterus due to pancreatitis are the other serious complications of this operative procedure. The authors repeatedly emphasize the importance of a thorough preoperative as well as postoperative ex-

ploration of the abdomen They definitely point out that of all the causes of icterus, liver deficiency is probably the most frequent

In postoperative *stenosis* (mostly pyloric and duodenal) subhepatic plastic peritonitis plays a great part It is just sufficient to replace or elevate the drain and see that the incident ceases Thorough exploration of the ductus choledochus, gall-bladder and pancreas is the main requisite before any surgical steps are undertaken If doubt exists as to the integrity of the common bile duct, a choledochotomy should be performed without hesitation, before anything else is attempted

The authors reveal some detailed but nevertheless important minor technical points, particularly emphasizing the necessity of placing separate ligatures on the cystic duct and on the cystic artery Among some of their highly recommended suggestions is always to close the peritoneum with the great omentum fixed to the inferior border of the parietal peritoneum At the conclusion they stress once more the importance of proper drainage, which is next in importance to a skillfully done cholecystectomy, and the value of combined cigaret drain and rubber drain. The latter facilitate hemostasis and isolate the operative zone

**Biliary Fistulæ.**—F H Lahey (Ann Surg 92 649 (Oct) 1930) reports 8 transplantations of complete external biliary fistulæ in addition to the 2 previously recorded Six of the patients are free from symptoms, 1 had a recurrence of the external fistula; 1 has had frequent attacks of intermittent biliary obstruction, and 2 died from the operation

The most important surgical principle in this operation is the preservation of

adequate vascularization. This is attained by leaving the fistulous tract attached to the undersurface of the liver. The tract is cored out from the abdominal wall down to its attachment to the liver. A short section of rubber catheter is inserted into the fistula and anastomosis effected between the stomach and duodenum or jejunum. If the anastomosis is made to the stomach, the latter is drawn through an incision in the omentum which has been reflected onto the hepatogastric ligament. The anastomosis is, therefore, essentially extraperitoneal. An incision is made into the stomach, and through a counter-incision the end of the fistula with its attached rubber tube is drawn into the stomach and sutured in position. The adjacent portion of the stomach is then fixed to the undersurface of the liver. If the duodenum or jejunum is used for the anastomosis it must first be immobilized.

In the 10 cases of complete external fistula reported by the author there were 4 internal biliary fistulæ, but as none of the spontaneous fistulæ between the stomach or duodenum were of sufficient size to prevent back-pressure and jaundice, it was necessary in each case to detach the internal fistula and establish a complete external fistula.

Spontaneous internal biliary fistulæ are at times the cause of failure of external biliary fistulæ to remain open until they are ready for transplantation. The author has prevented this complication by the extraperitoneal method of transplantation described.

As above indicated, surgical experience has shown that the stomach is best employed for the anastomosis, because it tolerates bile well and because, if a fistula occurs, it is less serious in the stomach than in the duodenum.

*Diagnosis*—According to I. Ginzburg and E. W. Benjamin (*Ibid* 91 233 (Feb) 1930), the *injection of lipiodol* constitutes a safe and simple method for the study of postoperative biliary fistulæ in the absence of active infection involving the duct system. The injections are best made under fluoroscopic control.

Biliary fistulæ which show no evidence of obstruction in the extrahepatic duct system close spontaneously. In the absence of obstruction distal to the internal opening of the fistulous tract, the lipiodol appears almost immediately in the duodenum and there is no reversal of flow into the intrahepatic biliary radicle. The presence of obstruction will prevent the lipiodol from entering the duodenum immediately and, if sufficient lipiodol is used, will result in a reversal of its flow.

When the stools contain bile, lipiodol may demonstrate the presence of incomplete obstruction. Such fistulæ may close spontaneously, but the encroachment upon the lumen will probably give rise to symptoms in the future.

The nature of the obstruction must be determined by inference. Obstruction in the hepatic or supraduodenal portion of the common duct is likely to be due to stricture, whereas obstruction near the papilla is more likely to be due to stone. The presence of a stone will not necessarily cause a filling defect in the lipiodol shadow.

Routine examination of biliary fistulæ lasting longer than 2 or 3 weeks may result in earlier diagnosis of structures of the ducts.

In the greatly dilated common duct frequently found a few years after cholecystectomy there may be delay in the passage of the lipiodol into the duodenum without the presence of obstruction.

In cases of complete biliary fistulæ, lipiodol studies may help to indicate the most feasible reconstructive procedure

### POSTOPERATIVE RESULTS.

—In the 500 cases of cholecystectomy reviewed by R. L. Sanders (*Ibid* 92. 376 (Mar.) 1930) the average age of the patient was 43 years. The youngest patient was 4 and the oldest 83 years of age. The mortality was 4 per cent.

In 78.2 per cent of the cases the chief complaints were epigastric pain, fulness, gas, and bloating. Gall-stone colic occurred in 59.2 per cent, but stones were found in only 40 per cent of the gall-bladders removed. Jaundice was present in 23 per cent and nausea and vomiting occurred in 51 per cent. Wound infection occurred in 6 per cent of cases with tight closure and 14 per cent of those with drainage.

In the cases with drainage there was a mortality of 6 per cent. The chief causes of death were pneumonia, myocardial and hepatic insufficiency, and shock.

The author believes that when the cystic duct and artery are tied together there is less danger of leakage.

All of the gall-bladders were studied by a pathologist. Only 5.8 per cent presented the mild type of cholecystitis. Strawberry gall-bladder was found in 10 per cent of the cases and relief was most marked after removal of this type.

The end-results in 352 cases were

	Per Cent
Complete relief of symptoms ..	84.0
Partial relief of symptoms ..	11.6
No benefit or symptoms made worse ..	4.0
Digestion much improved ... ..	87.0
Only partial relief ... ..	9.3
Digestion not benefited or made worse . . . . .	3.7
No colic . . . . .	87.2
Recurrent colic ..	12.5
No subsequent jaundice ..	95.4
One or more attacks of jaundice ..	4.5
Condition of wound satisfactory ..	91.4
Bulge or hernia .. . . . .	8.5

In 2 of the cases in which postoperative jaundice occurred, it was accounted for by the discovery of stones in the common duct, but in the others the cause was less certain.

Most of the unsatisfactory end-results occurred in cases in which there was cholecystographic evidence warranting operation, but not a good clinical history. In most of the cases in which no relief was obtained there was a mild cholecystitis.

R. D. McClure (*Ibid* 90. 253 (Aug.) 1929) believes that the incidence of *pneumonia* as a postoperative complication can be further reduced by sufficient dental prophylaxis immediately before the operation and by sending the patients to the hospital a day or two before operation to preclude the development of acute respiratory infection.

The incidence of *thrombosis* and *embolism* is more difficult to reduce as the cause of these conditions is not clear. Postoperative exercises as recommended by Pool and thyroid medication as recommended by Walters may be of value. The injection of an anti-coagulant at the time of the operation may be the best solution of the problem.

The author reports 4 deaths which occurred when a second incision was made for removal of the gall-bladder when the primary intervention was done in the lower part of the abdomen. He states that the practice of performing a second operation under the same anesthesia increases the mortality rate.

E. MacD. Stanton (*Am. J. Surg.* 8: 1026 (May) 1930) has analyzed the immediate causes of death in 500 cases in which surgery of the biliary tract was done. About 30 per cent of the deaths were due directly to the biliary disease. The biliary conditions included gall-bladder perforation, hepatic insufficiency,

ency, liver abscesses, and cholemia. Peritonitis accounted for 15 per cent of the deaths, shock and hemorrhage for 11 per cent, cholemia for 7 per cent; pulmonary embolism for 6.6 per cent; perforations of the gall-bladder and bile ducts for 6.5 per cent, pneumonia for 10 per cent.; cardiac conditions for 6.5 per cent; renal complications for 5 per cent, hepatic insufficiency for 4.5 per cent; metastatic abscesses for 3 per cent, gastric dilatation, protracted vomiting and intestinal obstruction for 3 per cent.; and acute pancreatitis for 1.25 per cent. Twenty deaths (3 per cent of the total number) listed as "high temperature deaths" are discussed in detail. Their cause is unknown. The fever often reaches 106° F (41.1° C.), and death ensued within from 36 to 48 hours after the operation. Stanton believes such deaths are "liver fatalities" and are probably as definitely associated with biliary surgery as postoperative hyperthyroidism is associated with goiter surgery. The clinical picture is that of an overwhelming toxemia.

Bile peritonitis as distinguished from septic peritonitis accounted for approximately 15 per cent. of the total number of deaths from peritonitis.

**BISMUTH.**—*Bismarsen* or *bismuth arspnenamine*, a combination of bismuth and arspnenamine, having an arsenical content of 12 to 15 per cent. and a bismuth content of 23 to 25 per cent, has been used extensively during the last couple of years and was recently reported upon by J. H. Stokes, T. H. Miller and H. Beerman (Arch. Dermat. and Syph. 23:624 (Apr.) 1931). It is given intramuscularly, once or twice each week, in doses of 0.1 to 0.2 Gm (1½ to 3 grains). The

drug already dissolved and ready for injection is available in ampules or it may be obtained in powder form and should then be dissolved in water containing butyn, the latter acting as an anesthetic, to minimize the unpleasant feelings attendant upon injection.

In a series of cases reported by these observers, 2 per cent showed slight pain, which yielded to hot applications and massage when the injections were troublesome to the patient. Eleven per cent of the series revealed mild systemic reactions such as nitritoid crises, gastrointestinal disturbances and cutaneous disorders. Stokes and his associates recommend that 2 injections a week be given in cases of early syphilis, and the effect on the Wassermann reaction should be repeatedly checked. They state that intermittent injections are less effective than continuous treatments, and further suggest that it is unnecessary to use iodides and mercury in conjunction with bismarsen. The Wassermann reaction of the cerebrospinal fluid was practically unaltered.

P. J. Hanzlik and H. G. Mehrtens (Arch. Dermat. and Syph. 22:850 (Nov.) 1930) studied clinically the absorption and excretion of numerous bismuth compounds which have been used in treating syphilis. They found that during the first 2 weeks following intramuscular injection of various bismuth compounds, the water soluble *bismuth sodium tartrate* in aqueous solution was more efficiently absorbed than the insoluble products used in oil or in aqueous medium, such as bismuth metal, potassium bismuth tartrate and bismuth salicylate. The urinary excretion of bismuth was studied in 11 human subjects, 4 of whom had cardiac edema. In the latter cases, excretion did not vary from that of patients with no



edema The bismuth excretion showed a prompt onset with an early peak, a comparatively short duration and no marked individual variation Usually, the day following administration it was also invariably present, showing rapid absorption The peak of daily excretion occurred on the second day and lasted about 13 days after single doses equivalent to 0.022 Gm ( $\frac{1}{3}$  grain) of bismuth were administered Several results were obtained when only 2 or 3 single doses were given, but when 17 successive doses were given a delayed peak was found The total excretion following the administration of 2 doses of bismuth, or 0.044 Gm. ( $\frac{2}{3}$  grain), was about the same, but the total excretion of bismuth after the highest doses used (0.2 Gm—3 grains—and above), as also the daily maximum of bismuth excreted, showed no proportionate increase to the increase in dosage, but, on the contrary, decreased, showing a similar tendency observed in the excretion of bismuth after the injection of bismuth metal discussed.

The intramuscular injection of soluble *bismuth sodium tartrate* results in prompt absorption, distribution and uniform excretion of bismuth as a rule, a prompt saturation of the tissues being thus produced If the medication be pushed, there is an accumulation of bismuth in the tissues because of the slowing down of excretion The rapid removal of bismuth points to the necessity of more frequent injections, but this should be utilized with suitable rest periods to avoid harmful effects of accumulation

The author states that deposits in the muscles following bismuth sodium tartrate injections are negligible, even though the bismuth is excreted in the urine for days in small amounts

Since so many various types of bismuth preparations are on the market, H N Cole, J E Moore, P A O'Leary, T Parran, Jr, J H Stokes and I S Wile (Ven Dis Inform (Public Health Service) 12:145 (Apr. 30) 1931) advise the physician to keep the following points in mind when selecting a preparation for use They state that the ideal form of bismuth should probably be one capable of rapid absorption from the site of injection, and yet not so rapid that there will be a diminished after-period of absorption It is important that the preparation be capable of exact dosage, also that it be not painful and not conducive to local abscess formation The ideal bismuth preparation should reveal by its excretion curve of metallic bismuth from the feces and urine that not only is it being absorbed, but that while some is stored in the system a certain appreciable level of bismuth is circulating continuously in the blood stream; also, finally, a good preparation should give good clinical results

The exact amount of bismuth required to produce an optimum level in the body is difficult to determine, but a preparation should contain from 0.03 Gm to 0.2 Gm. ( $\frac{1}{2}$  to 3 grains) metallic bismuth to a dose, and a course lasting from 8 to 10 weeks should amount to from 0.6 to 2 Gm (10 to 30 grains) of metallic bismuth These authors also call to mind the question that possibly it is not the total metallic bismuth that counts as the ionizable bismuth, and Cole indicates that attempts have been made to combine bismuth with certain other remedies

Stokes and Chambers have used a compound, *bismuth-arsphenamine-sulphonate*, intramuscularly which they recommend for the profession generally.

O'Leary and Brunsting have used this preparation satisfactorily for the past 4 or 5 years on about 310 cases and altogether have given over 5000 doses. They believe that the response in a limited number of their cases has not been substantiated by observations on a larger series. They describe a number of neurorelapses in patients. Cole and his colleagues remark that various French physicians are using liposoluble compounds with satisfactory results. The most common preparation is a *camphocarbonate* preparation with 0.08 Gm ( $1\frac{1}{8}$  grains) metallic bismuth per 2 cc (32 minims) and an alpha  $\alpha$ -carboxethyl  $\beta$ -methyl nonoate of bismuth, known in this country as *biliposol*. Excretion studies show that the liposoluble preparations give early and high bismuth excretion comparable to water-soluble preparations, but not as long as with the insoluble bismuth compounds. Furthermore, these injections are practically without pain and rarely cause abscess formation. Cole and his co-workers state that attempts to use bismuth by the inunction method have been disappointing, and they advise the intramuscular injections as the ideal therapeutic approach. They state that bismuth intravenously is 10 times as toxic as when given intramuscularly. In comparing the values of the various antiluetic remedies, Cole and his associates state that arsphenamine should be used for the case of fresh syphilis, to be followed later in the course of therapy by bismuth and mercury. In treating secondary syphilis, bismuth is a valuable adjunct, but should not replace arsphenamine.

**BLADDER.—DIVERTICULUM IN THE FEMALE.**—F. W. Schacht and J. L. Crenshaw (J Urol 24:393

(Oct) 1930) found only 18 cases of diverticula of the urinary bladder in females over a period of almost 20 years in The Mayo Clinic, the ratio of its prevalence in females and males being approximately 3 to 97. Thirteen were true and 5 were false diverticula. Three patients presented a urethral caruncle. 1 patient had a cyst 1.2 cm in diameter at the neck of the bladder of the false diverticula, 1 was consequent upon injury of childbirth and the other 4 were the results of operative procedures in the pelvis and abdomen. Infection of the bladder is often associated, as well as complications such as vesical calculus or neoplasm of the bladder. The diagnosis can nearly always be obtained by means of cystoscopy and cystograms.

**TUMORS.—Pathology.**—Tumors of the urinary bladder present a frequent and a difficult problem to the urologist. P. W. Aschner (Surg. Gynec. Obst. 52:979 (May) 1931) reviewed the slides of every tumor submitted to biopsy or operation at the Mt. Sinai Hospital, New York, since 1911. There were 90 cases of *papillomata* diagnosed on biopsy and confirmed by response to high frequency treatment, operative specimen and late results. New tumors or recurrences occurred in 23 per cent but they too were benign and responded to high frequency treatment.

In 7 additional cases, the original pathological report of papilloma was proved incorrect by subsequent developments.

In 4 cases of papilloma diagnosed by biopsy and corroborated, carcinoma of the bladder subsequently developed.

Of 285 bladder tumors, 142 or 50 per cent, were *papillary carcinomata* which, therefore, constitute the most numerous group of the common bladder tumors.

Of these 142 cases, 26 or more than 19 per cent were multiple tumors

Reliable information as to the nature of bladder tumors is obtained by cystoscopic biopsy in 97.5 per cent of patients. The biopsy material is of little value in prognosis. If a case simulates papilloma by cystoscopy and responds to fulguration, but shows malignancy histologically, active surgical or radium therapy is indicated.

The presence or absence of infiltration appears to be a reliable guide as to prognosis.

A case of carcinoma favorable for surgical treatment should receive segmental resection of the entire thickness of the bladder wall. Failure to do so, even in the pedunculated tumors, has often resulted in recurrence. Biopsy, however, is most essential before undertaking radical surgery as other lesions may resemble malignant growths.

**BLEPHAROSPASM.—TREATMENT.**—C. H. Frazier (Ann. Surg 93:1121 (June) 1931) reports a technic of nerve section which he employed with good results in 4 cases of blepharospasm. He found that the filaments to be isolated for section are not larger in diameter than strands of fine silk or hair filaments and that their number varies. Dissection, therefore, is tedious. A single filament at the level exposed might supply more than one muscle. The number to be cut must, therefore, be determined with the aid of electric stimulation. The immediate postoperative results have been eminently satisfactory. The etiology of blepharospasm is unknown.

**BLINDNESS.—ETIOLOGY.**—W. H. Wilder and A. M. Hayden (Am. J. Ophth 14:8 (Jan) 1931) have tab-

ulated the causes of blindness among those on the blind pension roll of the State of Illinois. The most frequent causes are opacities of the cornea, cataract, affections of the optic nerve, trauma and glaucoma. They advocate the organization in every state of a central commission for the blind and sufficiently flexible definitions of blindness to permit consideration of the character of the lesion and the visual fields. They criticize the definition of blindness embodied in the Missouri law which does not take into account the industrial blind.

The causes of blindness are summarized as follows.

Opacities of cornea	
From trachoma . . . . .	339
From other causes . . . . .	321
	— 660
Cataract in all forms . . . . .	716
Affections of uveal tract . . . . .	113
Affections of retina . . . . .	72
Glaucoma and complications . . . . .	295
Affections of optic nerve and complications . . . . .	595
Trauma . . . . .	388
Postoperative . . . . .	187
	— 3026
All other causes . . . . .	491
	— 3517

**Hysterical.—Diagnosis.**—A diagnosis of hysteria should not be based on any one symptom, but on the incongruity of the whole clinical picture. W. M. Alger (Am. J. Ophth 14:1057 (Oct) 1931) emphasizes the following points: (1) Sudden onset without obvious cause; (2) rapid variability of symptoms; (3) marked suggestibility of the patient; (4) cutaneous and corneal anesthesia; and (5) the contracted fields.

**BLOOD SUGAR.**—In an investigation bearing on the blood sugar changes in children following surgical

operation, R W Daffinee, J Garland and M G Gray (New England J Med 205 1182 (Dec 17) 1931) made blood sugar determinations before and after anesthesia in 20 children. Of these children, 17 were given ether in varying amounts, from 1½ to 11 ounces (45 to 330 Gm), 2 were given local novocaine anesthesia, and 1 spinal novocaine.

The blood sugar was higher following the operation in every case, irrespective of the length or character of the operation, or the mode of anesthesia. The amount of the rise varied from 7 to 69 mgm per cent.

The highest rise in blood sugar occurred in the case which received the most ether. It was in a 5 year old child, operated upon for tuberculous glands of the neck. The operation lasted 82 minutes, 11 ounces (330 Gm) of ether were used, and the x-ray of the thymus was negative. Before operation the blood sugar was 80 mg. per cent. After operation the sugar was 149 mg per cent.

M Young and H M. Turnbull (J Path and Bact 34 213 (Mar) 1931) studied the so-called status lymphaticus deaths to determine whether the thymus was the cause of these deaths or not, due to the fact that A B. MacLean and R C Sullivan (Proc Soc Exper Biol and Med 23 425 (Mar.) 1926) had declared that there is a similarity in the mode of death in cases of so-called status lymphaticus and cases of sugar shock from insulin overdosage.

Unexplained deaths in children could not be traced with any regularity to enlarged thymus. There was no arterial hyperplasia associated with large thymus glands. The amount of lymphatic tissue bore no relationship to the weight of the thymus. There is no proof that the so-called "status thymico-

lymphaticus" is a pathological entity. An abnormally large thymus is not an indicator of "status thymico-lymphaticus."

Three cases studied by Daffinee and his associates had enlarged thymus glands (by x-ray), and yet gave histories of having undergone previous operations without difficulty.

In 2 cases which were operated upon, each had a rise of only 6 mg per cent. of blood sugar during operation, from 94 to 100 and from 87 to 93 mg per cent respectively. The operations lasted 30 minutes and 44 minutes; anesthesia was local novocaine in 1, and 3 ounces (90 Gm) of ether by drop method in the other. No constant relationship exists between the amount of blood sugar rise and any of the following factors:

1. Disease requiring surgical operation
2. Age of the child undergoing operation
3. The character of the operation.
4. The duration of the operation
5. The mode and kind of anesthesia.

### BLOOD TRANSFUSION.—

Five hundred consecutive transfusions on 382 patients formed the basis for a study by W. K. Burwell (Am J Obst and Gynec 22 261 (Aug) 1931). Of these patients, 83 had received 2 transfusions, 14 were given 3, and 1 patient was transfused 4 times. Still another case with cancer of the uterine cervix was given 5 transfusions.

The bloods were matched according to the classification and hanging drop method advocated by Moss. The reviewer is of the opinion that too much emphasis should not be laid on the method of *typing* and *cross typing*. He states that no patient should be given a

transfusion without the serum being cross matched with the donor's cells, and that compatibility should not be handed down under 30 minutes. Any irregularity in the examining fluids, such as rouleaux formation should be looked upon with suspicion, and the test had better be repeated.

When a second transfusion is decided upon, fresh serum from the transfused patient must be once more cross typed with the second donor's cells, and it is wise to follow this practice routinely, even if the same donor is used.

Thirty-three per cent of Type II patients were found in this series of 382 cases, and 18 per cent of the group belonged to Type III. Seventy-five per cent. of the donors were of the universal type. In the series of cases reviewed, blood relatives were used as donors in only 20 per cent, and auto-transfusion was performed on 5 cases.

Five hundred c c of blood seems to be the *amount* generally agreed upon. In cases where severe hemorrhage and shock were present, however, the amount may be extended to 750 c c to 1000 c c. Blood counts were made immediately before and following transfusion, and 48 hours later, and the influence on the hemoglobin and red blood cells was noted. Within 48 hours, a change of the hemoglobin from 53.56 to 62.72 per cent, corresponding to an increase in the red cell count of from 3,295,000 to 3,736,000 was found.

The average *leukocyte count* before transfusion was 10,178 and 48 hours later it fell to 9,218. In cases where sepsis existed, the count fell from 15,185 to 13,188. If the severity of the infection be judged by the estimate of the leukocyte count, and improvement be looked upon as accompanied by a fall in the count, it seems plausible to

conclude that transfusions are definitely of value in these cases.

The *blood-pressure* appeared to be very little affected, either immediately or within 48 hours, in either of the systolic or diastolic readings. Two groups of patients were selected, (1) those with the systolic pressure between 100 and 130 in which no changes whatsoever in either readings were observed, and (2) those with a systolic pressure of 150 or over in which slight modifications were found, the systolic pressure averaging 164, 151, 150 and the diastolic 93, 87 and 89, for figures of the pressure taken immediately before, 2 hours later, and 48 hours following transfusion.

Except in the presence of chills, the effect on the *temperature curves* was not striking. The reviewer states that a rise of temperature, undoubtedly often does occur, exclusive of chills from the infusion *per se*, and in these cases, the causes are probably from protein sensitization and may have little or no effect on the picture itself.

Unless considerable blood has been lost at operation, transfusions for **post-operative shock** are likely to be unsuccessful, and these patients should be given *gum glucose* rather than whole blood. Especially is this rule to be followed when the patient is still under the influence of an anesthetic. Since an unconscious patient cannot furnish the danger signal, or signs of incompatibility, it is a wise precaution to wait until consciousness has returned before the patient is given a transfusion, and in all cases a hypodermic needle, filled with adrenalin, should be at hand, in case signs of incompatibility are found.

The chief *indications* for transfusion, in this observer's opinion, are: (1) **profound anemia**, after which he mentions *severe, rapid bleeding*; (2) **ane-**

mia as the result of sepsis; (3) straight sepsis; (4) traumatic shock. For the latter condition, he, however, recommends the administration of *glucose* rather than transfusion

*Reactions* on the part of the patient are divided into 2 parts, *i e*, (1) the immediate reactions occurring within 6 hours, and (2) the delayed reactions which appear in from 6 to 48 hours after transfusion. Reactions, however, may occur later, but are said to be rare and relatively unimportant. These, again, the writer subdivides as (1) single reactions, (2) multiple reactions, and (3) thrombophlebitis

Of the series of 500 transfusions reviewed, 270 were without any reaction. Single reactions occurred in 137 cases, but the author is inclined to avoid stressing the importance of these since, in his opinion, many would have occurred regardless of the transfusion. Fifty of the patients complained of severe headache, and 25 suffered from chills, which lasted from 16½ minutes to 29 minutes. Many of the patients complained, however, of ordinary chilliness. Restlessness, perspiration, nausea and vomiting are a common occurrence, and in these cases, urticaria, epigastric distress, diarrhea, backache and facial eczema were rarely found

Multiple posttransfusion reactions occurred 182 times in 72 patients, and the average duration of the chills were from 16½ minutes in the immediate stage, to 29 minutes in the delayed stage. Burwell (*loc cit*) states that no added danger is encountered when blood transfusions are repeated. Many of the patients had some cardiac affections such as a simple murmur at the apex or base, occasional slight enlargement, but signs of decompensation were rare. These patients all stand transfusion well.

However, if the cardiac disease is advanced, it is well to consult a cardiologist before transfusing

*Thrombophlebitis* occurred in 4 patients, in 3 of whom it followed operation and in the other case it was due to sepsis. Thirteen of the patients died soon after transfusion. All of these were extremely ill and were transfused as a last resort. Of the series of 500 transfusions, 1 death only occurred which was laid directly to the transfusion

The number of blood transfusions has greatly increased in recent years because of the great confidence and the reliability of the blood group tests, as pointed out by H. Wildegans (*Deutsche med. Wchnschr* 56 2031 (Nov. 28) 1930). Even in spite of these blood group tests, however, fatalities following the transfusions are more frequent than is believed, and this observer makes a critical review of the causes and finds mistakes that are due to carelessness and which could be avoided. He believes that when several transfusions are made at the same time, it is possible to mix the donors so that the correct matching is not followed out. Fatalities following upon errors in group testings may be eliminated if a control is made just preceding the transfusion.

It is also advisable to examine the serums closely at frequent intervals, so that mistakes caused by deterioration of the agglutinating serums may be avoided.

Before every transfusion it should be the rule that the serum of the recipient should be mixed with the red blood cells of the donor. Occasionally, errors in blood group determination may be caused by abnormalities in the blood groups, and a further complication may result if the blood of the donor is not



sufficiently diluted in the recipient. This occurs in cases suffering from marked loss of blood. Wildegans believes that the total amount of circulating blood should always be calculated or estimated before transfusion, and never more than one-sixth or one-fifth of the total quantity of blood should be transfused at one time.

*Mass transfusions*, using several donors, are also not advisable, unless injections with blood diluting fluids have preceded. In patients in whom the hematopoietic system is not functioning properly, the use of universal donors may cause a catastrophe. In order to ascertain if autoagglutination exists, which is frequently the case in hemolytic icterus, pneumonia, anemia, cachexia and syphilis, the serum should be mixed with a drop of fresh blood. Paragglutination, found in bacteremia and in chronic suppurations, may likewise prevent a correct determination of blood groups. *Fatality* following transfusion is usually due to the fact that the elimination of the foreign substances overtaxes certain organs, as the heart and blood vessels, kidneys and liver. *Thrombosis* or *embolism* following transfusion is not an especially grave danger if the technic is faultless, but cardiac dilatation occasionally may occur.

*Fatalities* from transfusion are more frequent when given for blood diseases and severe sepsis than for acute hemorrhage. Even with utmost care, it has happened that malaria and syphilis have been transmitted by blood transfusions.

Danger of *anaphylaxis* is present if, when repeated transfusions are essential, the same donor is chosen. In order to avoid this, a new donor of the same blood group should be used. The relationship between agglutination and hemolysis is still an open point. If

hemolysis may take place without preceding agglutination, then it would be necessary that in the preliminary tests more attention be given to hemolysis than has previously been done.

Seventeen patients are described by J. Bordley, 3d (Arch Int Med 47:288 (Feb) 1931) in which a *delayed or prolonged reaction* following the transfusion occurred. Three of these are cases reported for the first time and 14 have been selected from the literature. The reaction, as a rule, runs a peculiar and quite characteristic course with the following features: (1) Immediately after transfusion there is a sharp febrile reaction, followed frequently by hemoglobinuria and invariably by suppression of the urine. (2) Then an interval of several days exists, during which symptomatic improvement but continued oliguria is present. (3) After this interval the characteristic features of the delayed reaction come on rapidly and begin with agitation or drowsiness, replaced by outspoken evidence of anemia. Convulsions and coma may supervene at any moment. The outcome is very often fatal; 11 of the 17 cases reported died. Recovery is associated with diuresis, and death is due to uremia. At autopsy, the kidneys are found to be swollen, the tubular epithelial cells show drops of a peculiar pigmented material and advanced degenerative changes, the tubular lumens are filled with various cells, blood pigment and debris. Small necroses are very often present in the liver. Bordley summarizes the sequence of events as follows. A subject is given an injection of incompatible blood which damages the kidneys and in due time produces a uremia.

E. F. Grove and M. J. Crum (J Lab and Clin Med 16:259 (Dec) 1930) describe a case of a patient given a

transfusion of incompatible blood without reaction, and find a source of error due to contamination of grouping sera with "mustard bacillus" The patient was an 8-year-old group O who was given a transfusion of 300 c c of Group B blood, showing at no time the slightest reaction The authors believe that the absence of symptoms was due to the inability of the B isoagglutinin to clump B corpuscles at body temperature The transfused B corpuscles had entirely disappeared by the seventh day The transfusion was made with the incompatible blood due to a mistake in the grouping of the patient, and to contamination of the anti-B grouping serum with a "mustard bacillus," which organism causes a nonspecific agglutinating property for all human blood cells On this account, a routine check over of the usual method of grouping with known test sera is advised, by testing the patient's serum against freshly obtained A and B corpuscles, and also against Group O corpuscles

Antigen precipitation is only the first step of the complement fixation procedure visible, in the opinion of B S Levine (Am J Syph 15:81 (Jan) 1931)

The recent precipitation procedures utilized in the laboratory diagnosis of syphilis are relatively not greater as improvements over the earlier procedures than the old cold incubation complement fixation tests are over the early Wassermann tests The tests are not really specific for syphilis They are but empiricals as are all complement fixation tests None of the antigen precipitation procedures are any more sensitive at any stage of the syphilitic disease than are the properly standardized cold incubation complement fixation tests. Antigen precipitation procedures, simi-

lar to those of complement fixation, give positive reactions, of weaker intensity as a rule, with serum of individuals showing certain low grade affections other than syphilis Such reactions are valuable in the determination of suitable donors, although they are nonspecific from the point of view of diagnosis The tests for syphilis of the antigen precipitation variety have their zones of nonreactivities just as the complement fixation procedures have The serum conditions causing nonreaction either with the precipitation or with the complement fixation procedures, or with both, are intermittent as a rule The donor's serum should be tested at least 3 different times and by as many laboratory procedures as available. One set of tests should be performed immediately preceding the transfusion The test should include 1 warm incubation, 1 cold incubation and 1 precipitation procedure, and a searching clinical review of the donor must be made

L Burnham (Arch Int Med 46 502 (Sept) 1930) gives a full report of a case in which a Group II (A) blood was given to a Group III (B) recipient without a fatal reaction, which is usually the case The patient was a colored female, aged 35, weighing only 85 pounds, brought into the hospital requiring a pelvic operation A preoperative transfusion was thought necessary because a secondary anemia with 55 per cent hemoglobin and 3,400,000 erythrocytes existed. On typing, the patient's blood was found to belong to Group III or B The blood of the husband was grouped and seemed to be that of a universal donor, that is, it belonged to the Jansky Group I or O. Cross-matching of his cells against his wife's serum appeared satisfactory. The direct transfusion method of Scannell was used, and the

blood was given very slowly. After from 40 to 60 cc were given, the patient coughed and complained of some oppression in the chest and slight dizziness, but the pulse remained of good quality, the rate being 90.

As the symptoms seemed to increase gradually, the transfusion was temporarily stopped when she had received 200 cc, but after 5 or 10 minutes, seeming well, the transfusion was continued, whereupon recurrence of the coughing and oppression in the chest appeared. Immediately after transfusion, the temperature was  $99.2^{\circ}\text{F}$  ( $37.3^{\circ}\text{C}$ ), the pulse rate 90 and the respiration 24, 2 hours later, the temperature was  $101^{\circ}\text{F}$  ( $38.3^{\circ}\text{C}$ ), pulse rate 94 and respiration 20. This was the only temperature reaction found. At the end of 6 hours, the headache had entirely disappeared. The following day the patient felt well, blood showed 70 per cent hemoglobin with 3,850,000 erythrocytes and the urine was free from albumin, sugar and red cells.

The next day, a right salpingo-oophorectomy and appendectomy were performed. Because of the reaction, the grouping of the donor's blood was checked up, and this time the blood was found to belong to Group II (A) instead of to the universal donor group as previously classified. The author believes that the mistake in the first grouping and cross-matching was due to the use of a very dilute suspension of cells, together with failure to stir or agitate sufficiently the mixtures of widely separated donor's cells and test serum. In the hope of finding an explanation for the mildness of the symptoms, serologic examination was made.

Specimens of the blood were obtained from the patient on the third and sixth days following transfusion and classified

as 1 and 2. The results of the grouping with the usual test serums were different with the 2 specimens. When tested with Group III serum (anti-A), specimen 1 showed a few clumps in the midst of a great preponderance of unagglutinated cells. The mixture with Group II serum (anti-B) showed massive clumping of most of the cells with, however, a small number of cells lying singly and flat. The similar mixtures with specimen 2 showed no clumping in the test with Group III (anti-A) serum and no flat lying single cells in the test with Group II (anti-B) serum. Testing with specimen 2 definitely identified the recipient as a Group III individual, and the test with specimen 1 demonstrated the presence of the donor's Group II cells in small proportion in the recipient's blood. When the serum of specimen 1 was mixed on the slide with a 1:20 suspension of the donor's corpuscles at room temperature, there was a rapid massive clumping. This appeared surprising, since the demonstrated presence of unagglutinated donor's corpuscles in the blood had been made.

The paradox was explained by the following experiment. The same constituents were utilized but held at body temperature before and after the mixture was made. Examination of this mixture on a warm slide showed no agglutination until the slide began to cool, when complete agglutination took place. Both this agglutination on the slide and that which occurred when the mixture in the test-tube was allowed to cool were resolved on rewarming.

These experiments indicate that the patient's serum contained no specific agglutinins active at body temperature, but only a powerful property of agglutinating the donor's cells at room tempera-

ture or at a still lower temperature. In view of the well-known fact that cold agglutinins are usually not group-specific, *i e*, they act on the blood corpuscles of all groups, it is necessary to ascertain whether the strong cold agglutination shown by the patient's serum was due to the presence of such non-specific cold agglutinins, or whether, as is rare, the agglutination was caused by the group-specific  $\alpha$  which was capable of acting only at temperature lower than 37° C. (98.6° F). This question was answered by testing the patient's serum against a number of blood specimens of the different groups: 24 of Group I (O), 24 of Group II (A), 6 of Group III (B), and 4 of Group IV (AB). In no case was any clumping observed of Group I or III cells, and in every case the Group II and IV cells were strongly agglutinated at room temperature. None of the 3 blood specimens of groups tested at body temperature showed agglutination at this temperature. These tests identify the agglutinin as the group-specific  $\alpha$  acting only in the cold. No similar instance has been found in the literature, although the unanalyzed case of Jervell may have been of the same nature.

The author cites Landsteiner and Levine, who were successful in showing, along with the common iso-agglutinin, the existence of a fraction of the  $\alpha$  iso-agglutinin which was incapable of clumping Group II (A) cells at body temperature. In these experiments the cold  $\alpha$  was accompanied by the usual  $\alpha$  acting at body temperature. In a later paper, these investigators describe a Group (A) serum in which the B iso-agglutinin clumped B cells distinctly at room temperature but weakly or not at all, depending on the blood cells, at body temperature. Burnham concludes that

the mild symptoms shown by his patient during transfusion were due to some cooling of the transfused blood, sufficient to cause a mild temporary agglutination.

*Auto-agglutination* as a phenomenon is not common, and transfusion in such cases is still more rare. W. Stewart and E. E. Harvey (Lancet 2: 399 (Aug 22) 1931) were unable to find record of any instance in which transfusion was performed for auto-agglutination and because of this, 2 cases which they recently observed are described. In every case of blood transfusion, the blood matching was performed before transfusion was given, and the serum of the recipient was matched against the red-cell saline emulsion of the proposed donor. In both of the cases described, the serum of the patient agglutinated the red cells of the donor. The blood matchings were made at laboratory temperature. At the suggestion of Dr. Dyke, the slides used were transferred to the incubator (temperature 37° C) and it was found that the agglutination disappeared.

The first case was that of a married woman, aged 32, and 7 months pregnant, complaining of lassitude, headache, and noises in the head. Very severe hemorrhage from hemorrhoids existed. She was extremely pale and emaciated, some slight edema of the lower limbs was present, and while the heart was not enlarged, there was a soft apical murmur. The red blood cells numbered 1,040,000 and the hemoglobin was 18 per cent. Transfusion was considered advisable, but it was found that the serum of the patient produced universal agglutination. The patient was herself Group (B) or (III Moss) and she had been tested against 3 donors of Group (O) or (IV Moss). When the

slides were transferred to the incubator, however, the clumping in all cases disappeared. On testing the erythrocytes of the patient against her own serum, there was slight but distinct agglutination at laboratory temperature, and intense agglutination at ice-chest temperature, ( $4^{\circ}\text{C}$ — $39.2^{\circ}\text{F}$ ). Agglutination also occurred between the patient's serum and the red cells of all other Group (O) or (IV Moss) individuals at ( $4^{\circ}\text{C}$ — $39.2^{\circ}\text{F}$ ), although it was slow in coming on, but there was no agglutination when the matching was done at incubator temperature. Because of the fact that the patient could not possibly agglutinate her own red cells at body temperature, a transfusion was agreed upon, her husband, Group (O), being used as the donor. Fifteen ounces of blood were given by the sodium citrate method, precautions being taken to maintain the blood at body temperature during the procedure. Twenty minutes after the transfusion the patient collapsed and the temperature rose to  $104^{\circ}\text{F}$ . ( $40^{\circ}\text{C}$ ). She was extremely dyspneic and was scarcely able to tell that she was suffering from pain and distress about the chest. Following *tepid sponging*, and *morphine* and *adrenalin*, there was a cessation of all symptoms, with no further anxiety. On the days following transfusion there was no evidence of intravascular hemolysis or clumping of the red cells, and no hemoglobinuria or jaundice. The patient was given *iron* and recovered nicely. Within a month the hemoglobin rose to 61 per cent and the red cells 3,125,000. She was delivered of a full-term living child, and a few days after confinement she still showed the cold auto-agglutination of her own red cells, and also the red cells of Group (O) or (IV Moss).

The second case was that of a girl, aged  $5\frac{1}{2}$ , with **thrombocytopenic purpura**. A petechial rash appeared 5 days before admission, beginning on the face and spreading downward. Two days before admission bleeding commenced from the gums and nose, and there was also some melena and slight hematemesis.

At the time of admission, the patient was very anemic, blood was oozing from the gums and nose, and there was a slight generalized hemorrhagic rash. The breath had an acetone odor. Transfusion was suggested in order to stop the hemorrhage. On routine blood matching, the serum from the patient agglutinated the red cells of each donor tested. The patient herself was Group (A) or (II Moss), and her serum had been put against the red cells of her father, Group (A) (II Moss), her mother of a similar group, and those of another, Group (O) or (IV Moss). Agglutination occurred in all cases at laboratory temperature. The matching was repeated at incubator temperature and the clumping disappeared. As the condition of the patient was desperate, it seemed doubtful whether she could stand a reaction. However, it being an emergency, transfusion of 8 ounces (240 cc) of blood from Group (O), (IV Moss) was made. Three-quarters of an hour later the patient collapsed, temperature rose to  $105^{\circ}\text{F}$  ( $40.5^{\circ}\text{C}$ ), and marked dyspnea developed, the patient suffering from severe shock. *Adrenalin* and *morphine* were given and *tepid sponging* applied. Within a short time there was recovery and cessation of the hemorrhage. On the following day, the child developed a bronchopneumonia which ran a severe course, but in 12 days, the chest was cleared completely. While on admission to the hospital the

hemoglobin was 32 per cent and the red cells 1,520,000, about a month later the hemoglobin was 54 per cent and the red cells 3,730,000. The patient was discharged as being in a perfectly healthy condition.

The authors presented these histories to show that cases which manifest agglutination can be transfused. They state that the agglutination is apparently a temperature phenomenon and does not occur at body temperature. As a rule, the lower the temperature, the more intense is the clumping of the red cells. Because of this, it is essential that the blood of the donor be not allowed to cool during transfusion. In the event of a reaction, *morphine* and *adrenalin* should be promptly administered.

**BONE REPAIR.**—H. E. Pearce and J. J. Morton (*J Bone and Joint Surg* 13:68 (Jan) 1931), who have carried out an interesting study of the effects of alterations in the blood supply on bone growth, observed the effect of changes in the venous, the arterial, and the vasomotor systems on the healing process. They reached the conclusion that blocking of the deep veins producing venous stasis at the site of healing results in an increased callus formation and accelerated bone repair.

From additional observations they believe that obstruction of the lesser saphenous veins has no influence on the healing of the fibula. Blocking the arterial circulation by ligation of the main trunk has no effect because of the rapid development of collateral circulation. When the main artery and its branches are removed there is delay in bone repair, but healing eventually takes place. Removal of the lumbar sympathetic trunk and ganglia makes very little change in the process of bone repair in the extremity.

**BRAIN.—TUMOR.**—Daniel Kravitz (*Am J Ophth* 14:781 (Aug) 1931) discusses the *visual changes* in temporal lobe tumors and points out that the quadrant field defects are the most important localizing signs. Since large areas of brain space are devoted to the visual pathways they can readily be involved in many brain lesions. He reports a case presenting a quadrant field defect with papilledema and a rare occurrence in brain lesion—a divergence paralysis.

**BRONCHI.—BRONCHOSTENOSIS.**—E. Huizinga (*Neder maand v geneesk* 17:189, 1930) describes 6 cases of bronchostenosis in children resulting from a swelling of the hilus lymph nodes. In all 6 cases the manifestations began in an acute manner and the patients were sent to the clinic under the suspicion of the presence of a foreign body. The correct diagnosis can often be reached only by bronchoscopy. In 2 cases an acute lymphadenitis was involved, and in 3 or 4 cases tuberculosis was certain. In case of rupture, good therapeutic results can often be secured through bronchoscopy, either by the removal of granulations (2 cases) or by the elimination of a caseous mass in the more acute stage (2 cases). The most common place for the rupture is the point where the trachea merges with the right bronchus.

**CARCINOMA.**—E. E. Atkins (*J Path and Bact* 34:343 (May) 1931) concludes, from necropsy observations in 80 cases in men and 13 in women, that the mean age of male patients with primary carcinoma of the bronchus is higher when it is a squamous cell growth than when the cells are of other types, the respective mean ages being 51 and



43 3 years in his series Carcinoma does not appear to arise in one bronchus more frequently than in the other The order of frequency of occurrence of metastases in the abdominal organs was liver, pancreas, kidney, suprarenal and spleen In about half the cases no metastases at all were found The squamous cell carcinomas exhibit a great tendency to necrosis and liquefaction All the cases of definite cavitation found post-mortem in the growth were in squamous cell tumors The possibility that secondary deposits in the opposite lung are due to aspiration by way of the bronchus is suggested All such metastases in the series occurred in cases of squamous cell carcinoma with a marked tendency to liquefaction

From an analysis of 61 cases of primary carcinoma of the bronchus, E. H. Funk (J. A. M. A. 95:1879 (Dec 20) 1930) concludes that the clinical picture varies greatly, depending on the location of the neoplasm and the rapidity of its growth, the degree of bronchial obstruction produced, the presence or absence of secondary infection and suppuration, the pressure exerted on adjacent structures, the occurrence of pleural involvement, and the influence of local and general metastases The onset of the symptoms is usually insidious The most frequent symptoms are cough, expectoration, chest pain, hemoptysis, and dyspnea

F. R. Menne, M. Bisailon and T. D. Robertson (Northwest Med. 30:155 (Apr) 1931) report a clinical and pathological study of 16 cases of bronchogenic carcinoma They classify these cases into those of a hilar nodular and of a diffuse necrotic type The former, which were found in 62.5 per cent of their cases, are characterized by concentration of the nodules at the hilus

with a tendency toward mediastinal invasion The latter are characterized by diffuse dissemination of the nodules into the parenchyma of the lung with minimal concentration at the hilus

Microscopic study of the tumors showed a confusion of cell types so undifferentiated that their specific origin was not readily determined The primary bronchogenic carcinomata were found to originate, as a rule, from the primary and secondary divisions of the bronchi in the zone of the bronchial mucosa where the stratification begins to taper off into a single layer of epithelium In the authors' opinion, they probably never arise from the atrial epithelium

The tumors of the hilar nodular type were usually associated with symptoms which were referable to the lung, while those of the diffuse necrotic type were usually associated with symptoms which were referable to the pleura.

From a review of the literature, the authors conclude that there has been a definite increase in the incidence of primary bronchogenic carcinoma

**BRONCHIECTASIS.—ETIOLOGY.**—D. T. Smith (Arch. Surg. 31:1173 (Dec-pt. 2) 1930) asserts primary bronchiectasis is characterized by nontuberculous ulcerations and dilations of the larger bronchi with a chronic course, a distressing cough, and large quantity of sputum which may be very foul

The essential lesion, destruction of the elastic coat of the bronchus, is caused by focal necrosis, due to infection by the fusospirochetal group of anaerobic organisms, which include *Treponema macrodentium*, *Treponema microdentium*, *Spirocheta vincenti*, *Spirocheta buccalis*, *Vibrios* and *Cocci*. In active

cases the organisms are constantly present in the sputum and by suitable staining methods can be demonstrated deep in the tissues of the diseased bronchi. With this group of organisms bronchial disease comparable to bronchiectasis in man may be produced in rabbits.

Of 100 cases of nontuberculous bronchial disease, bronchiectasis was demonstrated in 60 by the iodized oil method. In 82 per cent of the cases of bronchiectasis the fusospirochetal group of organisms was found. In a number of the cases which were treated by **postural drainage** and repeated courses of **neoarsphenamine** or **sulpharsphenamine**, the spirochetes disappeared first, the fusiform bacilli and the vibrios next, and the cocci last.

Bronchiectasis may begin in one of 3 ways. In some cases a membranous exudate forms on the surface of the bronchial wall and ulceration takes place beneath this covering. More commonly, the anerobic organisms cause bronchopneumonia in which certain of the terminal bronchi are filled solidly with exudate. The organisms then invade the bronchial wall and cause bronchiectasis by destroying the elastic tissue support. In a third group of cases the bronchiectasis develops in the bronchi in which a lung abscess is draining.

In 8 of 12 cases which came to autopsy, spirochetes and fusiform bacilli were found in sections of bronchial dilations stained by Levaditi's method. In 4 of 6 other cases, fusiform bacilli were demonstrated in sections stained by Goodpasture's method.

In a series of 3 experiments on rabbits in which the simple aspiration method was used, fusospirochetal material from pyorrhea alveolaris, acute fusospirochetal bronchitis and pulmonary abscess caused bronchiectasis as

well as pulmonary abscess and gangrene. Control inoculations with pure cultures of staphylococcus aureus, aerobic hemolytic streptococci, anerobic hemolytic streptococci, streptococci viridans, anerobic streptothrix, Friedlander's bacilli, and influenza bacilli failed to produce permanent damage to the bronchi.

The author concludes that the fusospirochetal group of anerobic organisms are responsible for primary bronchiectasis.

Van Allen believes that spirochetal disease is not the cause of chronic abscess of the lung and bronchiectasis, but a secondary contaminant which is responsible for the chronic stages of the disease. He called attention to the fact that the rabbit is particularly susceptible to spirochetal disease, whereas the dog resists it. In the dog it is difficult to cause chronic lesions with spirochetes without producing an area of decreased resistance before implanting the organisms.

Hedblom stated that there are numerous causes for bronchiectasis, the most important of which are the acute infections occurring in childhood, bronchopneumonia occurring at any age, the various conditions that result in permanent atelectasis, and those that produce an extensive fibrosis of the lung, including fibroid phthisis. He cited Sauerbruch's opinion that involvement of the left lung is usually congenital. He did not agree with Lord's statement regarding the pathological changes, as many patients who have had bronchiectasis for years show little evidence of pathological processes in the parenchyma of the lung. He made a wise suggestion when he stressed the importance of preoperative prophylaxis of the mouth and throat with special regard to destruction of the spirochetes.

Lord, in discussing Smith's work, stated that it had caused increasing attention to be paid to spirochetes and fusiform bacilli as etiological factors in abscess of the lung. He said that, as a rule, bronchiectasis develops as a complication of a bronchopulmonary disturbance, and the pathological process in the lung is usually more important than the bronchial dilatation.

Smith (*loc cit*) described his work in isolating all of the organisms involved in abscess of the lung and bronchiectasis and then re-combining them to determine the combination necessary to reproduce the disease. He found that when the spirochetes were added to the coccus, vibrio, and fusiform bacillus, a severe lesion with an extensive necrosis and a foul odor was produced and the resulting disease could be transferred from one guinea-pig to another almost indefinitely. The spirochetes alone and the other organisms alone or in any combination without the spirochetes did not produce such a lesion. The spirochete is not secondary to the organisms, it is a concomitant rather than a secondary invader. Smith believes that Sauerbruch did not distinguish clearly between congenital bronchiectasis and bronchiectasis beginning early in childhood as an infective process. He emphasized the importance of **preoperative prophylaxis of the mouth and throat** and the use of **arsenic therapy and postural drainage** in the treatment of bronchiectasis. He agreed with Coryllos that atelectasis is a factor in the development of certain cases of abscess and bronchiectasis. He stated that the fusospirochetal organisms do not readily survive on the surface of the bronchus, they either disappear completely and leave no disease or they invade deeply into the bronchial wall, where they pro-

duce bronchiectasis by destroying the elastic tissue.

A Ochsner (Am J M Sc 179 388 (Mar) 1930) asserts that bronchiectasis occurs much more frequently than is generally assumed. The author believes it is the most common of all chronic pulmonary affections. It has been attributed to (1) congenital dilatation of the bronchi, (2) cirrhosis of the lungs; (3) chronic pneumonia, (4) alterations in the bronchial secretions allowing the growth of organisms which cause infection favoring bronchial dilatation, (5) acute infectious diseases, especially influenza, pertussis and measles; (6) infections of the upper respiratory tract, especially sinusitis, (7) loss of nerve control, (8) stenosis of the bronchi, and (9) chronic bronchitis. The author believes that the most frequent cause is chronic bronchitis.

**PATHOLOGY.**—Bronchiectasis varies from simple dilatation of the tracheobronchial tree to excessive dilatation with marked changes in the walls of the bronchi. In the advanced stages the elastic tissue and musculature of the walls of the bronchi become replaced by fibrous tissue. The author is of the opinion that the dilatation is functional and occurs primarily as the result of infection within the bronchial tree, the fibrosis being secondary. He has observed 4 cases in which bronchial dilatation demonstrated by x-rays disappeared completely after control of infection within the bronchi. The most frequent site of involvement by bronchiectasis is the left lower lobe.

**SYMPTOMS.**—The most common symptoms and signs of bronchiectasis are those of chronic bronchitis. By far the majority of persons suffering from bronchiectasis do not present the typical textbook picture of the condition. The

chief symptom is cough, which may or may not be associated with expectoration. There are relatively few other symptoms. The condition is often diagnosed as chronic bronchitis or recurrent acute bronchitis. The sputum is seldom profuse. Hemoptysis occurs in from 50 to 70 per cent of the cases.

**DIAGNOSIS.**—On physical examination the most important finding is the limitation of motion on the affected side. In early cases little else can be found. The diagnosis is made following the intrabronchial introduction of iodized oil. The author prefers the "passive" technic because of its simplicity and because it allows fluoroscopic observation of the mode of filling the bronchi.

**PROGNOSIS.**—L. Findlay and S. Graham (Arch Dis Childhood 6.1 (Feb) 1931) have had under observation since 1924, 32 definite examples of bronchiectasis. Twelve of the patients have died, 1 of a coincident tuberculous meningitis and 4 following operation for drainage of the lung cavities or attempted excision of the lung. The average duration of life after the inception of the disease in the remaining 7 fatal cases was 2.63 years. Of those still alive, 14 have been under continuous observation for periods varying between 3 and 6 years and it is from an analysis of these cases that the conclusion is drawn that the prognosis in bronchiectasis in childhood is grave, as the condition usually steadily gets worse and leads to a fatal termination. Undoubtedly, bronchiectasis following a chronic pneumonia may disappear, but only when the degree of dilatation is slight. The age of onset of the bronchiectasis would seem to influence the course of events; recovery is more probable in the cases that develop during later child-

hood. During childhood the duration of the illness is of no prognostic help.

**TREATMENT.**—Surgical treatment of bronchiectasis, according to Ochsner (*loc cit*), has not been entirely satisfactory. Drainage of the cavities has been abandoned except after cauterization pneumectomy. Collapse of bronchiectatic cavities is often rendered impossible by the fibrosis. In some cases operations on the phrenic nerve have been beneficial. The ideal procedure, at least theoretically, is removal of the diseased process. However, lobectomy is attended with a high mortality and should, therefore, be reserved for a relatively small group of cases. If lobectomy is to be attempted, the method of choice is the **cautery lobectomy** of Graham.

The medical treatment of bronchiectasis has been unsatisfactory. However, **postural drainage** is of benefit. The value of the dehydration or "thirst" cure is questionable. Since the use of iodized oil intrabronchially in the diagnosis of bronchial lesions, improvement has frequently been noted after this procedure. The author believes that repeated introductions of iodized oil are of distinct therapeutic value. He reviews 112 cases so treated. The largest number of fillings received by any of the patients was 16. The diagnosis of bronchiectasis was made in every case by fluoroscopic observation of the mode of filling of the bronchi. X-ray films were also made for confirmation and record. In 32 per cent of the cases a symptomatic cure was obtained, and in 12 per cent of this number there was x-ray evidence of cure. In 36 per cent of the cases there was symptomatic relief, but after an acute respiratory infection a temporary relapse occurred. Thirty-two per cent of the patients are

still under treatment, but showed improvement at the time of this report

The technic employed for the introduction of the oil was the passive technic, in which the swallowing reflex is abolished by the application of 10 per cent cocaine to the anterior surface of the anterior tonsillar pillars and the oil is aspirated from the pharynx into the tracheobronchial tree

R H Stiehm (Wisconsin Med J 29 556 (Oct) 1930) reports his results with iodized oil in 19 cases of bronchiectasis. Complete cessation of symptoms occurred in 33 per cent, improvement in 46 per cent, no improvement in 21 per cent. Complete credit for the results is given to the insufflations of iodized oil. Hygienic living, postural drainage, rest and the systemic effect from the iodine content of the iodized oil are all given consideration. Case histories show that patients treated with iodized oil do far better than those without treatment

R Nissen (Munch med Wchnschr 77 1849 (Oct 24) 1930) considers that many cases of bronchiectasis in children originate in congenitally dilated bronchioles and the condition only follows "prolonged pneumonia" comparatively rarely, treatment should, therefore, aim at compressing these bronchioles. In order to achieve this he plugs the thoracic cavity round the affected lobe with a mixture of paraffin wax, and reports that good results have followed this method. In a child 300 to 400 cc are required, and expectoration ceased completely in a number of cases thus treated, the scoliosis which almost inevitably follows extensive rib resection or artificial paralysis of the diaphragm in a child is avoided

For those cases in which the effect of paraffin plugging is not permanent,

Nissen advocates lobectomy, remarking that if this is carried out in several stages the risk is not excessive. Among 4 children thus treated there were no deaths, although in 28 adults the mortality was 10 per cent. Nissen has found pneumothorax treatment disappointing in bronchiectasis. If a low pressure was used, the alveoli alone were compressed and not the dilated bronchioles, higher pressure merely displaced the mediastinum, again without affecting the bronchiectatic dilatations

**BURNS.—PATHOLOGY.**—Different types of lesions in the central nervous system were produced by using the alternating and continuous electrical currents. O R Langworthy (J. Exper Med 51 943 (June) 1930) found that hemorrhages were common after alternating current shocks and a few hemorrhages were noted in the animals shocked by the continuous circuit. The most marked pathological changes were noted in the latter group, with injury to the cerebral and cerebellar cortices on the dorsal surface close to the electrode applied to the head. Small cavities were produced, especially in the cerebral cortex. The author concludes that death, in cases of shock from either direct or alternating current, is due to respiratory failure rather than to actual death of the cells

Death from a superficial burn has been held to be due to a toxin circulating in the blood. Each period of chemical advance has had its suggested toxin. In an experimental study by F P Underhill and R Kapsinow (J Lab. and Clin Med 16 823 (May) 1931), it was observed that extract of burned skin injected intravenously into 20 guinea-pigs caused the symptom complex of burn toxemia. Eight pigs died in convul-

sions Necropsy findings were similar to those seen in superficial burns

Further investigation and experimentation led to attributing the symptoms to alcohol in the extract and not to a toxin of the burned tissue Normal blood and blood of burned animals when injected intraperitoneally into test animals gave practically similar results and led to the conclusion that the blood of burned animals contained no burn toxin.

The conclusions reached were that the postulation of a "burn toxin" is unnecessary, since the symptoms and effects of a burn may be adequately explained by the establishment of blood concentration to a degree incompatible with life The large loss of fluid from the blood of the wounded area leads to the establishment of blood concentration. Therapeutic measures should be directed to the prevention or alleviation of shock and the maintenance of blood concentration of a degree compatible with life and to local treatment of the wound to prevent infection and to facilitate healing

In describing the effects of injury from *lightning stroke*, H Dengl (Munchn med Wchnschr 78:27 (Jan. 2) 1931) reports the case of a woman, who while working in the fields, was struck by lightning Physical examination showed a mark the size of a copper penny at the top of the head where the lightning had entered the body The hair on the head was singed, and along the entire course of the spinal column there was a mark from 25 to 30 cm in width, which was continued on the back of the thigh A second track of lightning branched off at the neck, and here there was a mark from 2 to 3 cm wide, as well as a similar mark on the left breast and on the left side of the

abdomen The pubic hair was singed and on the back several skin defects were noted, with a coagulation necrosis about 4 cm in diameter. Numerous areas of black discoloration were found Examination of the chest revealed very weak heart sounds, but nothing of consequence in the pulmonary field The patient being unconscious for 2 days, sensibility tests were of no value

Following prolonged **artificial respiration** and the use of **cardiac stimulants**, the patient regained consciousness, although retrograde amnesia with reference to the accident was present The patient complained of aches and pains in the region of the burned areas and she had chills On the sixth day, a **lumbar puncture** was performed in an attempt to alleviate the *headache* **Tannic acid ointment** was used on bandages for the skin lesions, and 3 weeks from the time of entry, the patient was discharged from the hospital with the burns showing a tendency to heal. The author is impressed with the fact that, although the lightning entered the body at the occiput and passed along the entire spinal column, no permanent nervous disturbances were found. He also points out that this case contradicts the theory that if a stroke of lightning passes near the region of the heart, either heart failure or severe cardiac injuries are the result From his observations, Dengl is of the opinion that neither the extent nor the location of an injury sustained by a stroke of lightning is a reliable basis for prognosis.

**COMPLICATIONS.**—The case of a child of 3 years, who was seriously burned by tipping boiling water over his entire body, is reported by L. Coenen (Nederl. maandschr. v. geneesk. 17: 235, 1930) The next day a tempera-



ture of 104.9° F (40.5° C.) developed and convulsions were present. The patient was comatose, the eyes being fixed toward the left and Kernig's symptom and stiff neck developed. The burns healed slowly, but manifestations showing changed conditions in the brain and the meninges were noted clinically. Previous to the burn the patient had had a bad fall. Disregarding this, the author is inclined to believe that the patient had an encephalitis which may have resulted from the toxic substances produced by the burns.

**TREATMENT.**—The statement that solutions of procaine hydrochloride-epinephrin cause unnatural conditions in the tissues, thereby diminishing tissue resistance toward infection, is not accepted by M. Novak (München med Wchnschr 77.1669 (Sept 26) 1930), who states that this is true only if, as solvent for the procaine hydrochloride, a neutral or weakly acid physiologic solution of sodium chloride is employed, since a solution would not be iso-alkaline with the blood otherwise. When a solution is used that has the alkalinity of the blood the results are favorable, this same opinion being held by several other investigators. Novak recommends that burns be treated by the immediate application of sterile cotton compresses saturated with the solutions designated, the compresses being changed in from 10 to 20 minutes. If the burns are deep, however, the compresses should be left on for about 3 hours. When this treatment is used the pain ceases almost at once, minor blisters disappear after a short time and the skin again covers over. At this stage the wound is dusted with iodoform powder. When kept aseptic, wounds heal without scars in 8 to 10 days.

In surveying the number of burn cases admitted to the Children's Hospital of Michigan during the past 3 years, E. C. Davidson (Minnesota Med. 13.775 (Nov) 1930) found that 52 per cent. of the cases showed that the burn was the result of someone leaving a pail of hot water unprotected, the filling of a bath tub with hot water and the child falling into it, or the child being burned from pulling a kettle of hot water, soup or coffee from a stove over itself. From these statistics it would appear that at least from this series of cases, more than 60 per cent. of the accidents were avoidable, and due directly to negligence or carelessness. The second important etiologic factor is that of children playing with matches or around a bonfire. Twenty-five per cent. of the cases in the series reported were of this origin. Tannic acid is used in the treatment because it lessens the toxemia, is analgesic and prevents the loss of body fluid, secondary infection is limited markedly by the absence of a favorable soil for bacterial growth. Scar tissue formation has been less marked, and the protective layer of coagulated protein forms a scaffold for the growth of the young epithelial cells over the denuded area.

I. Lloyd (Brit Med J 2.177 (Aug 1) 1931) points out that deaths from burns and scalds are subject to a corner's inquest in Great Britain, and with the improvements in housing, lighting and other hygienic facilities, beside the trend toward smaller families, a less number of fatalities has occurred in recent years, although there are still about 1700 yearly in England and Wales.

Scalds are said to be considerably more common than burns, and about 70 per cent. of the total number of deaths

from the combined causes are due to scalds. The first effect of a burn or scald is shock and the picture clinically differs in no way from that of shock due to other causes, the effect being due to blood stagnation in the capillary system throughout the entire body, with a consequent profound fall in blood-pressure such as occurs in fainting. Death, when it occurs, is due to a physical mechanism. Toxemia may come on with dramatic suddenness, Lloyd points out, when the patient appears to be doing very well. The temperature rises rapidly to as high as 104° F (40° C), there is an increase in the pulse rate, restlessness follows, passing into unconsciousness and death. Experimentally, this has been shown to be due to absorption of certain poisonous substances from the burned area. These substances are some form of protein, amongst which is histamine. The general treatment of a burn or scald is, of course, the treatment of shock primarily. When in severe agony, the patient should be given morphine hypodermically, and fluids by mouth in abundance. The author advises against the use of linseed and carron oils. Warm fluids and morphine are indicated as soon as possible. The use of a 2½ per cent aqueous solution of tannic acid, used since its original recommendation in 1925 by Davidson, has proven most satisfactory as far as local treatment is concerned. Toxemia being due to the formation of autolytic products of protein decomposition in the burned area, tannic acid coagulates the damaged proteins and prevents their absorption in the circulatory system, much as picric acid is said to do, therefore, with the prevention of absorption, the constitutional disturbances from absorption are minimized. Pain is diminished and

scarring appears to be generally slight in degree. Lloyd states also, that the mortality is reduced.

After being given a short time for some recovery from the initial shock, the patient is anesthetized with gas and oxygen and the burned area is carefully swabbed with ether. The dead and damaged tissue is cut away with scissors, vesicles are opened and their outer wall removed. A flat, clean surface is thereby obtained and tannic acid is applied in 2½ per cent freshly prepared aqueous solution with an ordinary throat spray.

The patient is returned to bed under electric lamps with no other dressing on the burns. The spraying is repeated hourly 7 or 8 times, until the burned area is tanned dark brown. Meanwhile, the toxins that have already entered the system are being diluted and removed by copious amounts of fluid given orally, subcutaneously, rectally or intravenously.

If this treatment has been promptly carried out, no sepsis is likely to develop. However, sometimes pus may form underneath the scab and fever will appear.

Lloyd warns against the use of fomentations or other moist dressings, which frequently have been employed and states that they are harmful, since they release the toxins from the inert coagulum and reestablish a condition of toxemia which it is most desirable to avoid. If fluid and pus collect under the crusts, the proper treatment is to liberate this pent-up fluid by cutting channels in the coagulum with pointed scissors and so providing mechanical drainage without moistening the scab. Meanwhile, the patient is kept beneath the electric light cradle which dries up discharge and maintains body heat.

The coagulum spontaneously separates in about 2 weeks, though when the burns are deeper it may take longer, and underneath the crust a healthy epithelium or granulation tissue is found which may be dressed with **flavine**, 1 1000 in paraffin, or with **sterile vaseline**, since the danger of toxemia has been eliminated

**Blood transfusion** has been advised, but since prevention is better than cure, if the toxemia can be prevented, no need for blood transfusion will arise. When, however, in spite of every effort and all possible care, the toxemia is well established, blood transfusion as an auxiliary method may prove life-saving

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## C

**CAFFEINE.—PHYSIOLOGICAL ACTION.**—The effect of caffeine on the cerebrospinal pressure has been studied by P G Denker (Am J M Sc 181 675 (May) 1931). This investigator utilized cases from the neurologic wards of Bellevue Hospital, New York City, the technic being as follows. After placing the patient horizontally on a flat bed, a lumbar puncture was made in the fourth lumbar interspace, a manometer was then attached and the spinal fluid pressure read. At first the pressure drops for a few minutes, but it assumes a stationary level at the end of about 5 minutes. As soon as this level was reached, as designated by the reading on the manometer, 5 grains (0.3 Gm) of caffeine sodium benzoate, in a sterile solution of 20 minims (1.25 cc) of water, were injected into one of the small veins of the forearm and the manometric pressure read every minute for 1 hour.

Notations were made of the respiration and blood-pressure throughout the experiment.

A definite decrease in the cerebrospinal fluid pressure was found in 49 of the 50 patients observed following intravenous caffeine injection, the average fall in pressure for all of the cases being 36 per cent, the maximum drop

68 per cent, and the minimum drop 8 per cent. In a series of 10 control cases, where a sterile solution of 20 minims (1.25 cc) of water with no caffeine was injected intravenously, no fall in cerebrospinal fluid pressure was noted.

Denker then speculates on the mechanism of spinal fluid pressure reduction by caffeine and approaches the discussion (1) from the action of caffeine on the circulation, (2) on respiration, (3) on diuresis. As to its *effect on the circulation*, the author quotes Sollman, who states that caffeine intravenously causes a fairly rapid fall in blood-pressure with prompt recovery. This fall of pressure, he believes, is presumably due to depression of the myocardium by the concentrated caffeine, and it does not occur when the drug is given orally or by other methods of administration.

Weed previously had demonstrated that a sudden rise in the arterial pressure could produce a sharp increase of corresponding degree in the cerebrospinal fluid pressure, and likewise the opposite obtained for a sudden fall in the blood-pressure. This is not the only factor of importance, as proven by the slow rate of return of the pressure to normal, as opposed to the blood-pressure, which rapidly returns to normal. Denker believes that the gradual ascent

would lead to a much longer duration of caffeine action than is to be expected if its effects were due entirely to momentary myocardial collapse with a quick recovery

In a series of cases examined by Denker, the blood-pressure was not found to change materially throughout the experiment. Denker quotes numerous observers, among them Roy and Sherrington, Wielchowski, Sollman and Pilcher and others, who are in agreement that caffeine produces a vasodilatation of the cerebral arteries, which is due, according to Wielchowski, not merely to a passive dilatation from constriction of the splanchnic area, but is a direct decrease of the tonus of the intracranial vessels. Since the brain is held in a fixed inelastic skull, this would produce a forcing out of the spinal fluid with a consequent increase in its pressure. The results, however, show that the exact reverse is what actually takes place, therefore, there is really something more to this mechanism than merely the circulatory action of caffeine.

The *diuretic action* of caffeine is accepted by all pharmacologists and therapeutists, even though this effect has not been experimentally demonstrated in cats or dogs. The diuresis is said to occur from an increase of flow concerning mainly the water content of the urine. Von Sobieranski, quoted by Denker, found that there was a marked difference in the effect of caffeine on dry fed and wet fed rabbits, and that in the absence of sufficient water in the tissues, caffeine diuresis does not take place. This is important with reference to intracranial pressure, since if the fluid content of the blood is decreased by copious diuresis, fluid will be drawn from the various tissues of the body, including the brain. To dilute the blood

to its normal consistency, Denker sums up the action as follows "diuresis, resulting in decreased water content of the blood, followed in turn by withdrawal of the body fluids into the blood stream to restore it to its normal viscosity. This dehydration, so to speak, causes a shrinkage in brain bulk with consequent decrease in spinal fluid pressure."

The *respiratory action* of caffeine is likewise pretty generally accepted by numerous experimental pharmacologists, and this action is important relative to intracranial pressure, since an excess of carbon dioxide in the blood causes an increase in the rate of secretion of the cerebrospinal fluid and *vice versa*.

Denker quotes Dixon and Halliburton, who believe that deficiency of oxygen or excess of carbon dioxide in the blood are the most important conditions influencing the cerebrospinal fluid secretion, therefore, if caffeine stimulates the respiration, causing a blowing off of carbon dioxide, with its resultant mild alkalosis, a decreased rate of secretion of cerebrospinal fluid takes place. Thus caffeine lowers the pressure of the cerebrospinal fluid by the combined pharmacologic actions rather than from any specific action directly on intracranial pressure.

Studying the diuretic action of caffeine by perfusion experiments on dogs, M. Morimoto (Ztschr. f. Kreislaufforsch. 21: 324 (June 1) 1929) noted that small amounts of the drug caused contraction of renal vessels. From his results, he is of the opinion that the diuretic property of caffeine is due to its action directly on the cells of the kidney parenchyma, rather than on the kidney arteries.

That caffeine is a powerful stimulant for the respiratory function was proven

in a series of experiments on dogs whose heads were isolated and whose respiration was retarded or arrested by injections of morphine or codeine. By injecting caffeine directly into the carotid artery, L. Binet and A. Arnaudet (Bull et mém Soc med d hôp de Paris 47·42 (Jan 26) 1931) were able to reestablish the inhibited respiration. While being somewhat reticent to express a preference for one particular medicine for use in stimulating respiratory action, these observers believe that caffeine should always be tried.

**THERAPEUTICS.**—Meyer and Gottlieb, according to Denker (*loc cit*), have prescribed caffeine with beneficial effects in certain cases of **headache**, and Sollman has found that fairly large doses of the drug are effective in headaches such as **migraine** and the **neuralgias**. The beneficial effects may have been due to a decrease in the intracranial pressure. Denker states that at Bellevue Hospital, on the neurological service, caffeine is used routinely to decrease intracranial pressure in cases of **brain tumor**, **fracture of the skull**, **cerebral hemorrhage** and similar conditions where there is an increase in the intracranial pressure. With headache in these cases, caffeine is most efficacious. Furthermore, in numerous cases of **essential hypertension**, more particularly those associated with an increase in spinal fluid pressure, caffeine may be more effective than amyl nitrite, or other vasodilators, in relieving severe paroxysms of headache which these patients so frequently suffer.

**CALCIUM. —ADMINISTRATION AND PREPARATIONS.**—A. L. Liebermann (J A M A. 97·15 (July 4) 1931) found that calcium in the form of *calcium gluconate* is the

most suitable from many standpoints. When given intramuscularly or subcutaneously, it causes practically no irritation. When given intravenously it produces a minimum amount of shock, but there is still the danger of formation of emboli and rapid death of the patient. When given orally, he found it best if administered about half an hour after a meal, as the calcium is better absorbed in the intestine in an alkaline medium in the form of calcium soap compounds. If given before a meal, too much acid may be present and the full value of the dose administered not obtained. In intramuscular therapy the blood calcium becomes highest 1 hour after injection. It must be remembered that calcium in any form, when given intramuscularly or intravenously, has a digitalis-like effect and may cause cardiac impairment. This effect, however, rapidly wears off and within 3 to 4 hours is totally lost. Calcium gluconate contains about 12½ per cent of calcium oxide. Other forms of calcium that are often used are the *lactate* and the *mallicate*. Most forms of calcium are extremely disagreeable to the taste, but the mallicate is rather palatable. In all cases, absorption is greatly increased when a high vitamin content is present. The dosage in calcium administration is best stabilized by carefully watching the output of calcium in the urine, with its ratio to the urinary phosphorus. In most cases this ratio should be about 1·5 to 1 or 2 to 1, and the total daily output should be at least 10 mgm (¼ grain) per kilogram (2½ pounds) of body weight per day.

**THERAPEUTICS.**—During the past year a great deal has been written about calcium therapy in its relation to the malnutritional diseases of childhood, to its effect on pulmonary tuberculosis,

its usefulness in the treatment of colitis, and its chemistry in general. Most of this work had been previously published and during this time has merely received verification.

One of the greatest successes in calcium therapy has been achieved in the treatment of children suffering from **vitamine D deficiency** and bone dyscrasias. G. Stearns (Am J Dis Child 42 749 (Oct) 1931) gives a lengthy discussion of the calcium-phosphorus retention ratio in infants and children and comes to the conclusion that 40 mgm ( $\frac{2}{3}$  grain) of calcium per kilogram ( $2\frac{1}{5}$  pounds) of body weight per day is desirable for artificially fed babies. About half as much phosphorus is necessary. In older children at least 10 mgm ( $\frac{1}{6}$  grain) per kilo ( $2\frac{1}{5}$  pounds) of body weight should be retained. G. Stearns and D. L. R. Moore (*Ibid* p 774) give a detailed case report which serves to substantiate these theories. It has been noticed that in children growing rapidly either in height or weight or both, the retention of calcium by the body is much increased over that in children whose growth is slow or stationary.

Eugen Baráth (M. J. and Rec 132 87, 139 (July 16, Aug 6) 1930) comments on the fact that **tetanic convulsions** in infants are accompanied by lowered blood calcium and that administration of calcium, in such form that it can be readily assimilated by the body, will quickly cause the convulsions to cease, if calcium therapy is persisted in, the baby will remain well. Stearns advises the use of *calcium in the diet* in connection with sufficient *vitamine D*, as she believes that the calcium is much better assimilated where the *vitamine* content is high.

The effect of calcium in **pregnant**

**women** was studied by A. Cantarow and M. Trumper (Surg Gynec Obst 51 469 (Oct) 1930). They found in normal pregnancy gradual diminution in the total serum calcium occurred. There was a slight progressive increase in the ratio of diffusible to nondiffusible calcium throughout pregnancy until the first stage of labor was reached. In the **toxemias of pregnancy** there was a marked decrease in the ratio of diffusible to nondiffusible calcium which in most instances seemed to be due to an increase in the nondiffusible fraction, and these authors believe that calcium therapy would be advantageous in this condition.

There has been considerable controversy regarding the use of calcium in the treatment of **pulmonary tuberculosis**. E. Undritz (Munchen med Wchschr 78 1741 (Oct. 9) 1931) believes that intramuscular calcium therapy should be carried out in all cases of pulmonary tuberculosis except in cases where the general condition is poor or the temperature is elevated. In those cases he feels that preliminary treatment with *camphor* should be given until the temperature has dropped and the general condition of the patient has been improved.

The theory is advanced by H. G. Scholtz (Beitr z Klin d Tuberk 78. 283 (Aug 20) 1931) that calcium is beneficial in the treatment of **pulmonary tuberculosis**, not because of any direct action on the diseased organ, but rather because it makes the blood-vessels less permeable and thus checks inflammatory processes.

J. B. Wolffe and S. Bellett (Ann. Int. Med. 4 795 (Jan) 1931) report 5 cases of **auricular paroxysmal tachycardia**, 3 of which were arrested by intravenous injections of *calcium*.



*gluconate* The reason for the improvement was thought to be that the calcium caused a prolonged refractory period in the auricular muscle and thereby gave the pace-maker an opportunity to resume its control of the situation. However, they state that there is no effect when the fibrillation is ventricular in origin.

Very little has been done to determine the action of calcium on the kidneys and circulatory system, however, W S O'Donnell and S J Levin (J A. M A 96 837 (Mar 14) 1931) used *calcium gluconate* subcutaneously in **edema with nephritis in children** and obtained very good results with the drug. They calculated that approximately  $7\frac{1}{2}$  grains (0.5 Gm) of calcium would remove 1 pound of fluid.

The administration of calcium is carried out in 3 ways, *viz*, intravenously, intramuscularly and orally. Most authors condemn the intravenous use of calcium except in great emergency and state that even then an effect can usually be procured with sufficient rapidity by intramuscular or subcutaneous injection.

B Haskell and A Cantarow (Am J Med Sci 181 180 (Feb) 1931) report a series of 13 cases of **colitis** in which calcium therapy was tried. Among these were cases of mucous colitis, ulcerative colitis and colitis due to spastic colon. In all cases of colitis it has been found that the diffusibility of calcium through the intestinal mucosa is increased. They do not attempt to correlate the 3 conditions under one heading, but find that all are considerably benefited when on a nonirritating diet high in calcium in utilizable form. In none of their cases has cure been permanent but the symptoms have been much relieved and remissions in the

course of the disease are much farther apart. Part of the value of calcium in the bloody ulcerative colitis is thought to be due to its effect in decreasing the coagulation time and, therefore, causing less hemorrhage, which in itself is irritating to the bowel. In the spastic colitis it is believed to be of benefit because of its stimulating action on the sympathetic nervous system, thus overcoming the vagotonia present.

**CAMPHOR.**—There has always been a disposition on the part of medical men to use camphor in some form or other as a cardiac stimulant when a patient is *in extremis*. During the past year considerable work has been done experimentally in an attempt to determine whether or not the use of this drug for such purposes has a sound scientific basis. H Busquet and C Vischniac (Paris méd 2 473 (Nov 29) 1930) find that many people show a tendency to local reaction from the subcutaneous injection of camphor. This reaction is not due to the olive oil which is used as a carrier, to any contamination that might be present, or to the camphor itself. They come to the conclusion that certain persons are more sensitive to this drug than others and that the local reaction noted on subcutaneous injection is an allergic phenomenon. Heimberger (Klin. Wchnschr 8 2238, 1929) carefully studied the effect of camphor on the peripheral circulation. His investigations were performed on normal persons in whom camphor and its substitutes were injected locally into a finger and the peripheral circulation then studied. He concluded that there was no effect, either dilatant or constrictive, on the vessels in question, but stated that this could not be accepted as final because

he firmly believed that in pathological conditions such as vasomotor collapse, the vessels were prone to react in a different manner. It is a moot question whether or not camphor has any actual action on the heart muscle, but it is thought that it acts as a cardiac stimulant.

Fox (Arch Otolaryng 11 48 (Jan) 1930), in commenting upon the use of camphor as a nasal spray in the acute infections, concluded that continuous application of camphor in a 5 per cent solution was apt to produce degenerative changes in the nasal mucous membrane. However, he found that the same changes were produced by eucalyptol, menthol and by liquid petrolatum. His experiments were done on rabbits and the application was carried out daily for 9 months. Sufficient work has not been done on the human nasal mucous membrane to be sure that the same effect would be procured.

**CAMPIODOL.**—Campiodol is an iodized rape-seed oil containing approximately 43 per cent of elemental iodine, with a specific gravity of 1.289. This is an extremely stable compound, very slightly irritating, and has a very low degree of toxicity. It has been used quite extensively in radiographic exploration of the lungs, spinal canal, cranial cavities, sinuses, for visualization of the Fallopian tubes and in genitourinary work. C. H. Frazier (Ann Surg 89:801, 1929) gives an interesting summary of its use in neurological x-ray work and states that in his opinion it is an extremely satisfactory solution. For his work he has used a mixture of 4 parts campiodol and 1 part ethyl olive oil. The olive oil is used only as a diluent, as undiluted campiodol has been found to be more or

less irritating to the central nervous system. Campiodol has no tendency to collect around the spinal roots and produce a false block, as is sometimes seen with other iodine preparations. One great advantage of this solution is that it is very quickly assimilated by the body and all x-ray pictures must be taken within 1 minute of injection or all trace of the opaque substance will have disappeared. The exact manner of assimilation by the organism is not known but in no instances have oil emboli or other detrimental effects been encountered.

M. A. Glaser (Am J Roentgenol 24:477, 1930) states that campiodol can be used extensively with very little danger to the patient. Experiments on dogs show that they will stand an oral dose as high as 6.75 cc ( $1\frac{3}{4}$  drams) per kilo ( $2\frac{1}{2}$  pounds) of body weight or 1.5 cc (24 minims) per kilo can be injected intravenously before danger is encountered. He has found the solution valuable in urography where a non-shadow forming stone has been lodged in the ureter. In some cases, an emulsion of campiodol and acacia has been used, but this would not be universally satisfactory except in urological roentgenology.

**CANCER.**—Cancer is the great scourge of modern civilization. The solution of this problem represents the most important factor confronting the medical profession today. Notable results followed the application of the hygienic principles instituted at the recommendation of scientists who pointed out the relationship between the mosquito and malaria, the rat and plague, the hookworm and hookworm disease, the spirochete and syphilis, unsanitation and tuberculosis, deficiency of diet and pellagra, rickets and the other

affections resulting from inadequate nutrition

In no other realm of human interest have the contributions to the welfare of mankind been so numerous and so beneficial as in the realm of medical science. In the march of progress, one after another of the agencies capable of altering or destroying and shortening human life have been brought under control, yet while substantial satisfactions have crowned the efforts of explorers in the field of medicine, a vast uncharted sea remains to be analyzed and brought within the realm of human knowledge.

Outstanding investigators all over the world are directing their best efforts to enlarging the sphere of information regarding the fundamental nature of cancer. Brilliant minds, as Carrel, Francis Carter Wood, Blair Bell, Gye, Reimann, Hammett, Bloodgood, Warthin, McFarland, Greenough, and many others, are intensively following likely pathways of approach to the ultimate recesses of biological phenomena in which province may be found the secret to explain the essential nature of growth, cellular embryology, morphology, metabolism and reproduction. The activities of cells are being observed and altered experimentally under varying conditions rigidly controlled. To understand the difference between growth, benign, integrated, organized and naturally controlled, in contradistinction to growth, malignant, destructive, disorganized and uncontrolled, is to define the nature of cancerous growth.

In the October 13, 1931, issue of Health News released by the United States Public Health Service, it is pointed out that the advances in sanitary lines which have been made against the hazards of the first decades of life, seem to have preserved the individual

only to make him subject to the liability of death from cancer, which apparently is steadily increasing, at least for the period in which American vital statistics have been available, or since 1900. In the year 1900, when the registration area was first organized, the crude death rate from cancer was 62 per 100,000 population. In 1920 it was 83.4 and in 1929 it was 96.1, an increase over the crude death rate of 1900 of nearly 52½ per cent. In the year 1929 there occurred 111,569 deaths from cancer, which makes this scourge second only to heart disease as the most important cause of death.

The external forms of cancer, *i e*, of the mouth and breast have shown a striking increase in the death rate, even though the diagnostic errors are low when compared with diagnosis of cancer of the stomach or other internal viscera.

The Public Health authorities are at a loss to explain the cause for this increase, but state that since the physical, chemical and biological changes all tend to establish a state of equilibrium, they venture to hope that the cancer death rate will not continue to grow, but, even in the absence of discovery of preventive measures, will sometime become stabilized. Because of the increase in the cancer death rate, research into the nature of cancer should certainly be stimulated. Cancer is said to be at first a local disease in which something goes wrong with the regulating mechanism of the body cells, causing an unwholesome persistent growth which, when it once begins, cannot be controlled; curatively, therefore, it must either be removed or destroyed locally.

Cancer is, of course, more likely to occur after the age of 35 than before and, therefore, the death rate in certain age groups is higher than in others.

Among all deaths between the ages of 45 and 70 in males, 1 in 8 is due to cancer, among women between 45 and 65, 1 in 5 is caused by cancer. The stomach, with 38 per cent of the total deaths, represents the most frequent site of fatal growth. Cancer of the breast caused 9 per cent of fatal cases, and cancer of the skin, 3 per cent. While a certain susceptibility to the possibility of cancer exists among members of some families, cancer is said not to be hereditary, although to the present time, this is an open issue.

In the release of December 19, 1931, United States Public Health Service, in discussing the *prevention* of cancer, states that if cancer at its onset were as painful as a sting, many people would promptly consult a physician and so receive the needed treatment early. Unfortunately, there is no pain or inconvenience in the early stages of many growths and symptoms develop only gradually. When a lump or mass, no matter how small, appears and persists for some time without some satisfactory explanation, patients should immediately consult a competent physician, and even though in the majority of cases the suspicion of cancer will prove unfounded, the patient will have availed himself of the most safe procedure.

In individuals over the age of 35 years, having a sore about the tongue, mouth or lips which does not heal, cancer should be suspected. Attention should likewise be directed to a spot where a tooth is broken or where an ill-fitting dental plate has rubbed a sore, furthermore, any irregular bleeding or abnormal discharge from a body orifice should be promptly investigated. Persistent indigestion with loss of body weight accompanies the cancer of the stomach. Procrastination in the face of

persistence of symptoms cannot but prove fatal if the nature of the disturbance within the body is finally revealed as cancerous.

This is regarded as one of the most important measures behind the movement for physical examinations at periodic intervals. It should be kept in mind that many cases of cancer can be cured and many may likewise be prevented when the general public will finally yield full cooperation to the medical profession which is endeavoring to eradicate this plague.

W. H. Kraemer (Am J Roentgenol 25 793 (June) 1931) points out that 70 per cent of persons attacked by cancer die from its effect and that the other 30 per cent are patients in which the cancers were found and treated before the growth had gotten beyond control.

W. B. Coley (Am J Surg 14 605 (Dec) 1931) states that at the International Lake Mohonk Conference held in 1926, and the International Cancer Conference held in London, in 1928, where delegates from all over the world were in attendance, no new light was thrown upon the fundamental problem, *i.e.*, the etiology of cancer, and that nothing new was offered concerning more effective measures for controlling cancer or checking its rising mortality.

Coley cites Ewing, who states that prevention plays a prominent rôle in the control of cancer. Ewing is of the opinion that *heredity* cannot be dismissed from a practical consideration of the origin of cancer, and states that the public should be apprised that when a strong tendency to cancer exists in a family, the other members should take unusual precaution against the disease. Ewing then goes on record as committing himself against the theory of cancer being a parasite, since it is incom-

patible with known facts concerning new growth. He does not believe that cancer is a single disease, such as syphilis or tuberculosis, and is of the opinion that it is made up of a great group of diseases of varied origin and course. Ewing states that the principal forms of cancer are due to some form of chronic irritation. Early diagnosis alone is insufficient to accomplish the desired reduction in the death rate. The experience of patients with early cancer who are cured has been very severe, while the fate of those who have not been cured is passed over silently. This is known and consequently any plan of solving the cancer control problem might lean heavily upon prevention.

Since the avoidance of chronic *irritation* is too often avoidance of the occupation or routine activity of the individual, it amounts to requesting that a presumptive cancer applicant give up his work and live the life of leisure, which is, of course, not practical.

Statistics on the possibility of recovery of patients with cancer, which statistics have been given by numerous clinics throughout the country, have been most disappointing. At St Luke's Hospital, in New York City, Shore, quoted by Coley, found that 68 per cent of 1000 patients were found inoperable when coming to the hospital and many others died of recurrence. Wood, in a later discussion, surveying 748 cancer patients, found only 21.8 per cent of 135 patients in which a mechanically removable mass was found at the time of examination. If these statistics represent the results obtained by men of unusual skill and experience, the average results throughout the country must be even more gloomy, therefore, the pessimism of the laity appears justifiable. Another discouraging fact in connection

with cancer control is that more than 50 per cent of all cases develop within the abdominal cavity, and when diagnosed have usually progressed so far that the diagnosis is made only to justify the diagnosis *per se*, with no hope of curing.

The best available statistics show no more than a 2½ per cent of 5-year cures in carcinoma of the stomach.

Coley (*loc cit*) concludes that continuous propaganda should be resorted to in order that patients consult physicians as soon as a tumor is discovered. He also advocates more detailed information for physicians handling these patients. A considerable amount of the funds raised for cancer control should be directed to collecting more facts, especially more accurate information as to the geographical distribution, and for data that may explain the wide variation in incidence. Coley recommends a more extensive probing of the hope, therapeutically, from x-ray and radium. Also, he advocates further serological studies, since in his hands the treatment of inoperable tumors, especially sarcoma, by the use of toxins of erysipelas and *Bacillus prodigiosus* have at times been successful. Inasmuch as a large number of these patients, beyond hope of cure from any other method, can be cured by toxins, and in many operable cases the toxins have been used as a prophylactic after operation, and a larger percentage of patients have remained well for 5 years, Coley, therefore, advocates more general adoption of this method.

Undergraduate students in medicine should be given better clinical instruction in the early diagnosis of cancer. Institution of a large number of cancer clinics throughout the country and the principal cities, as recommended by Ewing, is a wise move. These institu-

tions should have a large endowment to make them educational centers. Research laboratories in the whole field of cancer should be encouraged and assisted. An International Cancer Congress every 3 to 5 years, bringing together the leading workers in cancer and furnishing an opportunity for an interchange of ideas should be encouraged and developed, and the widest publicity should attend the work of these men.

**INCIDENCE.**—In the various countries where reliable statistics are available, W J Mayo (Ann Surg 93 16 (Jan) 1931) points out that the incidence of cancer, except for Egypt, is about the same with reference to the population and sex ratio, although the organs or tissues show considerable variation in frequency of involvement. Thirty per cent of cancers in females involve the breast and the uterus, and 30 per cent of those in the male involve the stomach and the genitourinary tract.

P Schrumpf-Pierron (Bull Acad. de méd Paris 105·818 (May 19) 1931) has investigated the reason for the rarity of cancer in Egypt. Among 19,529 deaths, in 1891, at Cairo, only 29 were due to cancer, or a percentage ratio of 0·09, while during the same time the proportion of deaths due to cancer in France was 4·6 per cent, and in England 4·3 per cent. From 1918 to 1928 inclusive, in Egypt, the average number of deaths from cancer was 0·23 per thousand. In Egypt, only 6 out of every 1000 deaths were due to cancer. In Italy, the average is 47·99. Even so, Schrumpf-Pierron believes that the figures for Egypt were too high, since only cities with a population of more than 5000 were studied, and he states that cancer is much more rare in the country than in the cities. The second

reason why the author believes that these statistics for Egypt are too high is that there is a special cause of cancer, *Schistosoma haematobium*, which is rare in Europe.

By studying the records of Egyptian hospitals, this observer noted that cancer of the gastrointestinal tract was very rare compared with a relatively high number of so-called mesenchymal tumors. Sarcomas are found to be about as frequent as epitheliomas. Many of the sarcomas are of the lymphosarcoma type. The author also points out that ulcers of the stomach, pylorus and duodenum are as rare in Egypt as cancer of the stomach. He believes that climate has something to do with this, since he states that a tropical climate prevents cancerization to a certain degree. Also, the race predisposition has to be excluded. European and American Jews appear to be predisposed to cancer, while it is practically unknown among the Egyptian Jews, even though they live in the same manner as the native Egyptians.

Analysis of the Egyptian soil shows that it contains 15 to 17 times more magnesium than soil from one of the most fertile fields of France. The waters of the Nile show from 6 to 22 mg of magnesium per 1000 cc. Schrumpf-Pierron believes this is why the Egyptian peasants who live in the country and drink the unfiltered Nile water rarely have cancer, whereas the inhabitants of large cities who drink filtered water are frequently affected with it. The frequency of cancer, so this author believes, is *inversely proportional to the richness of the soil in magnesium*.

**Sex Incidence.**—The recorded mortality rate from cancer about the middle of the past century was rather more



than double the number of cases occurring in female patients as occurred in male. However, there appears to have been a gradual diminution in this ratio and about 5 years ago the ratio became approximately equal, as pointed out by Sir George Newman, more recently, however, the ratio for males has slightly increased over that for females (Ministry of Health Reports on Public Health and Medical Subjects No 59, 1930; Practitioner 125 555 (Oct) 1930).

The Ministry of Health of Great Britain gives periodic reports on the nature and the kinds of cancer, and recently published one directed to a survey of the sites of cancer in men, with special reference to the lip, tongue and skin.

*Cancer of the lip* is found to be 12 times commoner in men than among women, and there appears to be no difference between smokers and non-smokers, except that old clay pipes and other methods of smoking prone to cause burns or epithelial damage may play a part by producing a chronic irritation.

In contrast with cancer of the tongue, cancer of the lip runs a slower course, the lower lip being much more frequently involved than the upper lip, the proportion being 95 to 5 per cent respectively. Information available concerning the duration of the disease, including the best methods of treatment, gives a survival rate of 76.1 per cent at 3 years following treatment.

*Cancer of the tongue* is 10 times commoner in men than in women. The mean age is about 54 years, rather less than in cancer of the lip, which is 57 years; while the mean age at death for tongue cancer in Great Britain is 61 years, or 9 years earlier than in cancer

of the lip. Data was not available to prove the frequency of lingual cancer in patients suffering from syphilis. Of all the patients operated, from 20 to 25 per cent of those suffering from cancer of the tongue were alive and well 3 years after operation, and the statistics point to the radiological method of treatment as being rather more satisfactory than operations.

*Cancer of the skin* is found more frequently among those individuals having an outdoor occupation. The reviewers are of the opinion that sunlight alone has little if any relationship to the occurrence of cutaneous malignancy. They point out that workers exposed to extreme heat such as puddlers, brick-makers and glasshouse workers exhibit a relatively higher death rate from cancer of the skin than other persons not so exposed. Treatment of the skin shows a survival-rate 3 years postoperative of about 40 to 50 per cent and of those treated by radium, of 80 to 90 per cent. Cancer of the skin is slightly more frequent in men than among women.

*Cancer of the scrotum* among chimney sweeps is designated as mule-spinners' cancer or an occupational disease. *Cancer of the penis* is rare and seldom seen in Jews and Mohammedans. It appears to be in some way related to phimosis and was present in 133 out of 271 patients. In a series of 649 cases, 11 patients were under 20 years of age, and 6 were over 80. The average age appears between 52 and 54 years.

**Multiple Primary Cancers.**—Multiple primary cancers occurring in the same individual are rare, but have been observed. They occur, as a rule, several years later in life than single carcinomata, as originally pointed out by

Eglin F R Hanlon (Am J Cancer (supp) 15 2001 (July) 1931) found among 3000 postmortem records at the Mayo Clinic a series of 18 cases of multiple primary carcinomata. Among the 3000 postmortem examinations 950 of the deaths were attributable to malignancy. Seven hundred and ten were carcinoma. In order to make the diagnosis of multiple primary carcinoma, the chief reliance must be placed on the difference in the microscopic appearance of the various tumors. In Hanlon's series, each tumor was studied in its possible relationship to a metastatic tumor mass and in every instance the effort was made to rule out metastasis. An excessive lapse of time between the appearance of the tumors with evident absence of metastases, and the distinct variations in the appearance of the lesions histologically, pointed toward the duality of the tumors. Of the 18 cases of multiple primary carcinomata, 13 occurred in males. Hanlon expresses himself that multiple primary carcinomata probably represent incidental occurrences more likely than as a definite response to a law of malignancy formation. The distribution appeared to follow the frequency of occurrence of single cancer growth. Sex incidence has not been discussed.

Multiple primary foci of cancer may develop separately, but may be related as shown by D A. Welsh (Med. J. Australia 1 282 (Mar 1) 1930) in 3 different ways, *i e* 1 As illustrated by the growth of multiple separate epitheliomas, chiefly of the basal cell or rodent type on areas of skin exposed to strong sunlight. This may be taken as an example of a cancer in which the continuous operation of an irritant over a long time produces multiple primary foci of similar, but not always identical, growth

at different times and places. The origin of one focus may be independent of the origin of another, except that they may be related to the operation of a common irritant, acting on a common tissue, as sunlight on skin, having a common biochemical predisposition, as lack of pigment.

2 The multifocal origin of cancer throughout a gland like the prostate where the whole gland undergoes a compensatory adenomatous overgrowth which may develop into a carcinoma of the uniform type, more or less simultaneously at separate foci throughout the gland substance. This is an example of a general biochemical stimulus operating on the whole epithelial content of the gland, because that gland acts as a single physiologic unit.

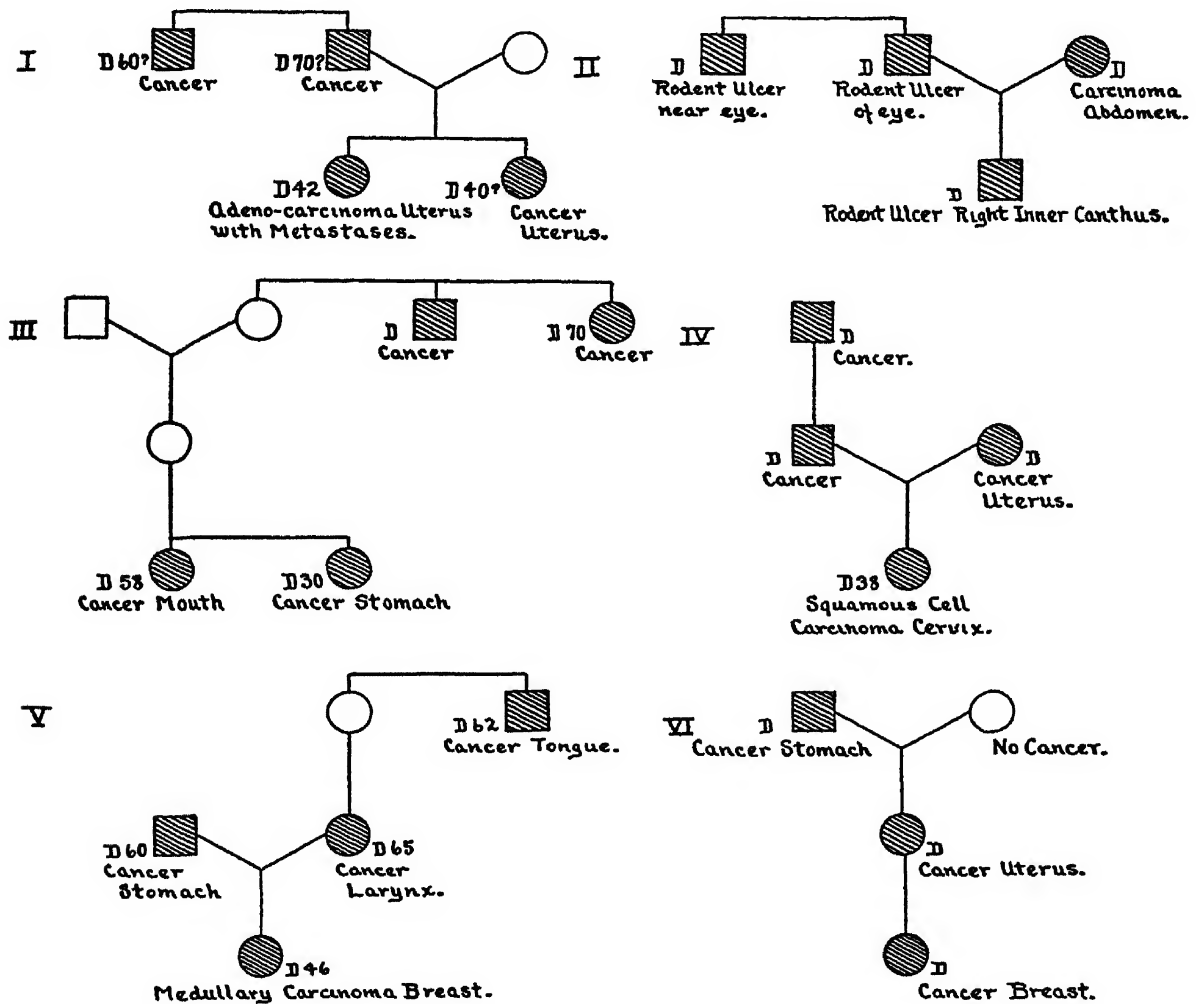
3. The discontinuous dissemination of the cancer-promoting material, as in the case of the lower lip.

**ETIOLOGY.—Heredity.**—In a brilliant discussion of the possible hereditary characteristic of cancer growth, A S Warthin (Ann. Int. Med. 4:681 (Jan) 1931) states that in a review of histories of surgical patients in a hospital, he found that in the ordinary run of case history, less than 1 per cent of such cases gave any family history at all. When, however, these same cases were probed by form letters or personal communications with the family, the percentage was raised to over 50 per cent. Warthin states that asking the patient himself directly concerning the possible occurrence of cancer in other members of the family is likely to give negative information, since the patient himself has about the same attitude toward revealing any family history of cancer as he has toward any history of syphilis or other sexual diseases. A fear exists of the stigma attached to a family

history of multiple incidence of malignancy. Of more importance, however, is the fact that few persons in the average hospital population really have a detailed knowledge of their family history back of the immediate parental genera-

quency of both positive and negative incorrect diagnoses.

Some years ago, Warthin investigated 330 cases of cancer, which revealed that over 60 per cent showed a multiple incidence of carcinoma in different gener-



Example of "Cancerous Fraternities" Multiple family incidence of cancer  
A S Warthin (Annals of Internal Medicine)

tion. The importance of the constitution and of heredity susceptibility is not as yet appreciated by the average practitioner or medical teacher of the present era, and this statement is supported by the inadequate case histories made by the average hospital physician. Likewise, cancer statistics are of diminished importance, because of the great fre-

quency of both positive and negative incorrect diagnoses. In the remaining 50 per cent. of cases with a negative history, Warthin states that the failure was due almost entirely to the ignorance of the patient or the family concerning the family history as far as cause of death of various members was concerned. That a positive history of multiple incidence of cancer could be obtained in 50 per cent.

of the cases certainly strongly indicates the hereditary side of malignancy.

In his studies, Warthin (*loc cit*) found that in certain families the carcinoma cases developed in every generation, indicating a direct inheritance, while in other families, the cases of cancer might miss 1 generation or 2, and appear in collateral lines and not in direct line. Those generations showing multiple occurrence of cancer cases Warthin designated as cancer fraternities or cancer generations as shown in his chart, revealing that cancer may be passed on directly or collaterally, and may appear in every generation or in every other one or second generation.

Certain families show so many incidences of cancer that they may be designated as cancer families.

In Warthin's studies of the multiple incidence of neoplasms, he points out the tendency of carcinoma to be localized in certain organs or systems, as the gastrointestinal or the genitourinary tracts. For example, in a particular family the males involved may show carcinomas of the gastrointestinal tract and the females carcinoma of the sexual organs, particularly of the breast and uterus. In this way, there is apparently a local organ or tissue susceptibility inherited. In 1 family, the great grandfather died of gastric cancer; the son also died of the same disease after marrying a woman who died of cancer of the breast. Six children of this union all died of cancer: 3 daughters of cancer of the breast; 2 sons of cancer of the stomach, and another of abdominal cancer not precisely located. The youngest son of this group married a woman without a history of cancer, and 1 child of this union, at 36, died of cancer of the uterus. Concerning the possibility of dominance or recessiveness of

the carcinoma factor in human families, it appears that in some families there is a dominant inheritance, while in others it is recessive. The variation in susceptibility found in different members of the same family may be explained by the complexity of the cancer character. It cannot be a single simple Mendelian character, but must consist of a combination of a large number of factors.

Warthin states that from available evidence, 2 conclusions are certain, *i e.*, (1) a constitutional susceptibility, and (2) a local organ-predisposition to cancer. The first shows that a patient may develop cancer, the second determines the organ or tissue in which it will grow.

Facts concerning inherited neoplasm susceptibility.

- 1 Multiple incidence of neoplasm in family generations.
- 2 Dominant inheritance of neoplasm in some families.
- 3 Recessive inheritance of neoplasm in some families.
- 4 Sex-limited inheritance of neoplasm in some families.
- 5 "Durchschlag" inheritance of neoplasm in some families.
- 6 Appearance of neoplasm independently of extrinsic factors.
- 7 Appearance of neoplasm at early age.
- 8 Multiple incidence of neoplasm affecting some organ or system.
- 9 Resistance or nonsusceptibility to neoplasm in some families.
- 10 Different degrees of susceptibility in the same family.

Summary of the facts known about inheritance of tumor susceptibility.

Interpretation of the facts relating to hereditary transmission of cancer rests upon at least 4 factors, in the opinion of Warthin, *i e.*, (1) a normal constitution resistant to blastoma; (2) the pathologic blastoma constitution; (3) the normal resistant organ or tissue make-up; (4) the pathologic organ predisposition to cancer. Each of these factors is

composite and not one is a simple Mendelian unit. Each represents large and complex genes in which a hundred or thousand subsidiary factors may enter and which may mendelize independently or in combination. Warthin states that the old conceptions of dominant and recessive characteristics have lost their original significance as far as inheritance of neoplasms in man is concerned. He also states that practically the individual who has a single case of cancer developing in 2 or 3 generations of his family need have little fear of himself developing cancer, but in the case of a person with a family history of a multiple incidence of cancer in several generations, a close watch should be maintained. Warthin emphasizes the importance of collateral lines, with reference to multiple incidence of cancer, rather than in the line of direct descent.

An individual with a history of multiple familial incidence should avoid all of the known extrinsic agents associated with causation of malignancy. Chronic irritation of any form should be obviated. The individual should not smoke or engage in any industry where he may be exposed to mineral oil, tar, paraffin or other irritating products. He should never be exposed to irradiation. Scars of the skin, particularly large scars from burns, should be treated by skin grafting. Whatever developmental anomalies might exist which could be corrected, should be corrected or removed. Rough pigmented moles should be removed and all chronic inflammatory conditions occurring in a person should be healed as quickly as possible.

The question of mating, as a general preventive measure, is of primary importance, and the man with a history of multiple incidence of carcinoma

should not marry a woman who has the same sort of family history. The preventive measures of eugenics should not be disregarded.

G. H. M. Waaler (*Norsk mag f laegevidensk* 92:557 (June) 1931) studied approximately 6000 cases dying of carcinoma, with especial interest in the cause of death among the immediate relatives of these patients, more particularly the brothers and sisters, husband or wife, and parents. From the information thus obtained Waaler drew the following conclusions and made this hypothesis: Two hereditary factors exist independently, which produce a disposition to cancer, each one of these tendencies appearing with a frequency of about 16 per cent. One is equally present in men and women and the other is more often found in women, also it must be admitted that cancer not infrequently is present in men without these factors but is less often present in women without them. Recessivity appears more probable than dominance, although to what extent, it is impossible to state. Thus cancer occurs more frequently among brothers and sisters than among married individuals and indicates, in Waaler's opinion, an important and significant hereditary predisposition.

The record of an entire single strain of mice derived from the mating of a cancerous female and noncancerous male, and bred through 3 generations, is recorded by M. Slye (*Am. J. Cancer* 15:2675 (Oct) 1931). Two hundred and seven individuals made up the entire strain, of which 115 were female and 92 were males. Of these, 23 were cancerous or slightly over 11 per cent. of the 207. This is a close approximation to the percentage occurrence of cancer in man. The types in this strain were cancer of the mammary gland,

squamous-cell carcinoma of the skin, carcinoma of the lung and leukemic diseases. Two external factors of importance were noted in connection with the 2 predominating types, *i e*, (1) chronic dermatitis of the muzzle and eyelid skin in both males and females, (2) a marked tendency to the formation of cysts in the inguinal mammary gland. The cases of skin cancer and every precancerous condition of the skin developed on the chronic dermatitis which frequently was of long duration, and several of the mammary gland cysts seem to have given rise to mammary gland carcinoma. Pneumonia and nephritis were also present in this strain of animals studied by Slye, and there was a tendency to emaciation in all of middle and late life, and a tendency to longevity. The average age when cancer was noted was 10 months and 1 day. The average age at death of the cancerous mice was 1 year, 1 month, 12 days, while of the noncancerous it was 1 year, 3 months, 29 days. Thus it is seen that the noncancerous mice lived longer than the cancerous, and the noncancerous offspring lived longer than the cancerous offspring. Among the 4 generations observed by Slye, the 23 cancers were distributed as follows: (1) in the parent generation, the female parent was cancerous; (2) in the first generation, none of the 9 individuals were cancerous; (3) in the second generation of 36, 9 were cancerous, and (4) in the third generation of 160 individuals, 13 were cancerous. These figures point to the classic expectation for cancer as a mendelian recessive.

**Susceptibility.**—Cramer is cited by J. A. Shaw-Mackenzie (*J Trop Med* 33:117 (May 1) 1930), who is also of the opinion that freedom from cancer is more likely to be obtained by diminish-

ing the susceptibility to it, than by trying to hunt down various forms of chronic irritation. Shaw-Mackenzie states that 25 years ago he surmised that cell proliferation or alteration of the type of division may be dependent on some systemic condition, but that local irritation, however, determines the site of growth. He points out that variations in the action of serum on the ferment lipase may be found in cancer and other diseases. When normal serum is added to pancreatic extract, or to the secretion itself, fat-splitting is markedly accelerated. Serum does not split fat, but it contains an activator. When carcinoma serum is added, the fat-splitting is diminished; therefore, the serum contains some inhibiting factor. Where recovery has been noted in patients, the action of the serum promptly returns to normal or is increased. In the opinion of Shaw-Mackenzie, therefore, the increased lipolytic activity is a factor which prevents the development of cancer and favors its disappearance when present. It is also associated with the resistance of the body to malignancy. Failure of response in an organ, other than that affected by cancer, may be a possible factor in causing the condition, also, as the result of deficient digestive ferments, the cells of any focus of lesser resistance would become overcharged with peptone, glycogen, fats, carbohydrates, etc., thus approximating the fetal type of cell with its reproductive cellular activity. Shaw-Mackenzie also discusses the various factors as those inhibiting the local aspects, the developmental factor, fatty acid in immunization, and other reactions of cancer in relation to diagnosis and the treatment of this disease. Shaw-Mackenzie discusses the results of Murphy and Leitch in producing tumor



growth by chemical substances from normal tissues and states that the substance isolated may be of the nature of an inhibitor or paralyzer of normal enzyme action, a direct ferment action not being concerned. In conclusion, the author points out that considerable alteration in the metabolism of fats and lipoids occurs in the blood and tissues of patients with cancer.

As pointed out by W J Mayo (Ann Surg 93:16 (Jan) 1931), cancer is never found in sound tissues. Chronic irritation, by making an opening for the possible entrance of microorganisms to the body, would appear to suggest an external agent, but this does not explain why malignancy develops in certain cases in which the sources of chronic irritation are slight if at all present, nor in other cases in which the sources of chronic irritation are very extensive for long periods of time. Furthermore, Mayo states that it is difficult to explain why the metastatic growths are the same as the tissues from which they originate, rather than resembling those tissues of the organs secondarily involved.

Mayo stresses the fact that individuals vary in their susceptibility to the cause or causes of cancer. He states that it is impossible to explain why 90 per cent of persons do not have cancer and 10 per cent die from it. It seems just as logical to accept the hypothesis that the 90 per cent have greater resistance to cancer than that the latter percentage come in contact with the hypothetical etiological factors. The measure of the body's resistance is the stroma about the cancer cells, and the greater amount of stroma and the less the number of cells, the slower is the cancer growth. Also the greater the proportion of cells and the less their re-

semblance to the normal tissue involved, the more rapid is the growth. All there is to cancer is contained within the malignant cells which have a remarkable resemblance to the rapidly growing embryonic cells of the chorionic villi (Langhan's cells). Mayo discusses the work of Murray on tar painting, of Gye and Barnard on the transplantation of the Rous sarcoma, of the work of Slye on mice cancer, and that of Bowing and Desjardins on the effect of radium and the x-ray in diminishing the malignant character of the growth, and states that these findings all point to a local and general susceptibility as perhaps the controlling factor in the genesis of malignancy. He states that the problem is one of increasing resistance to cancer in susceptible individuals.

**Physical Nature.**—In studying the physical nature of cancer cells, G W Crile (Am. J. Cancer 15:2659 (Oct) 1931) and his colleagues have looked for evidence supporting the widely held theory that cancer owes its development to some alteration in the cells as the result of mechanical, physical or chemical factors. With this in mind, they have been searching for some principle of a physical nature which would explain the conversion of normal cells into cancer cells as the result of single or repeated injuries. Cancer cells do not originate in uninjured, unchanged tissues, but rather in tissues that have been subjected to chronic irritation. It is also well known that the cancer cell owes its development to the operation of existing laws of growth within the host, since cancer originates and lives only in the living being, therefore, the problem resolves itself into a struggle for survival between the cancer cells and the normal cells, and the logical point of attack would seem to be in studying the char-

acteristics of the normal cells. This is in accord with the work of Hammett and Reimann. Crile has been studying the physical differences of cells which might possibly explain the conversion of differentiated into undifferentiated cells, and of cells whose energy is used primarily for function into cells whose energy is used primarily for growth. Compared with adjacent cells, the cancer cells appear to have a greater conductivity and capacity. In rat cancer, Crile has shown the injury current of a cancer is opposite to that of the neighboring tissues and viscera, and the electric potential may be an index controlling the treatment. The sign of charge of a cancer cell may be changed by ionization, and the change can be maintained.

**Irritation.**—In reviewing the increase in knowledge of cancer growth that has been revealed within the last several years, W. H. Woglom (Am. J. M. Sc. 181:157 (Feb.) 1931) states that certain important facts have been noted, as for example, that cancer has been found to occur frequently in fishes, that it has been found in all forms of animal life down to the reptiles at least; that it spares neither the herbivora nor the carnivora; and that meat is not an especially important factor.

Civilization likewise may, in the opinion of Woglom, be disregarded as an important possible cause, for as the primitive races and their physical characteristics are increasingly revealed, it appears that they too suffered from this dread curse.

Chronic irritation, so Woglom points out, is the one possible cause that has withstood the light of critical opinion. This seems to have some really essential relationship to the inception of malignancy. In recent years it has been possible to subject this hypothesis to ex-

perimental inquiry, and Woglom reviews the history of the work which serves to concentrate attention upon chronic irritation as an important factor in etiology.

Johannes Fibiger, in 1907, while studying tuberculosis in Copenhagen, noted an intense thickening of epithelium in the mucous membrane lining the pro-stomach in 3 wild rats. This thickening resembled a fibroepithelial growth, and was caused by a parasitic worm. Following this lead, Fibiger sought the relationship between this worm of the nematode group and the fibroepithelial growth. In 61 rats obtained from a large sugar refinery, 40 were hosts to this particular worm, and in 18 of these 40 this hyperplasia of the mucous membrane lining was present. By feeding experiments, Fibiger was able to produce a chronic irritation which led to the inception of cancer, thereby establishing the experimental production of cancer, for which Fibiger received the Nobel prize. Woglom also reviews the brilliant researches of K. Yamagiwa, of the Tokyo Imperial University, who, with his collaborator Itchikawa, was able to produce a tumor growth in the ear of a rabbit by the painting on of tar. By painting the ears day after day and month after month, over a year later they found malignant growth in the ears of certain of their experimental animals.

Carcinoma is notorious in human beings subjected to known irritants for a period of time, as carcinoma of the bladder in individuals working with aniline dyes; of the skin in the early x-ray workers, or of those daily exposed to tar and similar materials. It appears that about one-fifth of the life span of an individual is required for the inception of malignant disease, and Woglom

states that about 15 years would elapse between the beginning of chronic irritation and the appearance of a new growth, although many exceptions to this rough statement occur, as, for example, where cancer has followed a splash of hot tar within a few weeks or months. In order that malignancy may be initiated, the irritant must be exactly adapted to the tissue, the relationship of which is still unsolved. Woglom states that tar promptly produces cancer in the skin of man, mouse and rabbit, but not in the skin of the dog, guinea-pig or rat. In the author's opinion, it would be a fine thing if from tar, that portion could be isolated which incites malignant growth. However, of the several hundred constituents going to make up tar, not more than 100 are known; also the composition of tar varies, depending upon the coal from which it is distilled.

In examining the characteristics of the cancer cell, certain general facts are known, although no deviation from the normal cell has been as yet revealed. Numerous attempts have been made to find some variation between the cancer cell and its normal prototype. The hydrogen-ion concentration of cancer cells has been investigated, and it has at various times been said that the blood of cancer patients was more alkaline than normal blood. As a matter of fact, in spite of considerable careful work, no significant difference can be found between the serum of patients with early malignant disease and a group of non-cancerous patients. The only characteristic of the cancer cells so far discovered is its egoism—a sort of impudent independence, as Woglom states, which cannot be weighed, measured or as yet explained. It reveals itself, not in rapid growth, as bacteria and embryonic cells

grow, but more in a remorselessly steady proliferation.

Woglom's summary of the recent advances in the study of cancer are so clear cut and self explanatory that they are here quoted verbatim:

"An experimental approach to the problem of malignancy has been available for only 30 years, yet please remember that before the end of the first 10-year period the limits within which malignant tumors can be transplanted had been mapped out, a method of protecting against their inoculation found, the resistance of the cancer cell to various agents compared, its cultivation *in vitro* begun, the hereditary nature of cancer in mice foreshadowed, and a curiously interesting transmissible sarcoma of the fowl discovered and described.

"In the second decade the growth rate of the cancer cell was assessed, and 2 methods of producing tumors in animals were discovered, although it had been said that this would never be accomplished, and in spite of the fact that this period was disrupted by a world-wide war.

"In the third, still another means of inciting a malignant growth was reported, and a good start made on such problems as the chemical nature of the carcinogenic agent in tar, the intensity and duration of irritation required to initiate neoplasia, the relation of age to the development of cancer, and so on, while positions gained during the first 2 decades were consolidated and extended. I cannot but believe that in this experimental period of 30 years, representing only 1 per cent of the 3000 years during which cancer has been under observation, vastly more than 1 per cent of our present knowledge of cancer has been acquired."

**Occupation.**—A high incidence of *skin cancer* has been found by L. D. Haagensen (Am. J. Cancer 15:641 (Apr) 1931) in employees of *gas works*, resulting from their exposure to tar, and among *petroleum refinery* workers, as a result of their exposure to crude oil and its distillation fractions. Occupational exposure to *lubricating oil*, as for example of mechanics and machinists, predisposes to cancer of the penis

and scrotum, a predilection site best explained by the lack of cleanliness of the external genitalia so frequently found among laborers. Haagensen is of the opinion that *sunlight* has some bearing on the etiology of skin cancer, since he finds outdoor workers especially showing cancer of the face and lower limbs. This observer points out that lymphatic leukemia may result from exposure to radium. He believes that workers in proximity to x-rays and *radioactive substances* should have a blood count each month, since changes in the blood picture are not infrequent. Metastases occurred in 63 per cent of his cases of occupational x-ray cancer, which proved that this form is more malignant than is generally believed. Cases of cancer of the lung and cancer of the bladder apparently have no association with occupation. There appears to be a high incidence of skin cancer in some groups, such as clergymen, where the occupational risk is not apparent, therefore, as Haagensen points out, the occupation exposure is only one of the probably multiple etiologic factors of cancer.

Two clinical histories are discussed by O. Schurch (Deutsche med. Wchnschr. 57:139 (Jan. 23) 1931) describing 2 men with *cancer of the scrotum* who had been employed in *cork brick factories* for a period of more than 10 years. The bricks were made of pulverized coal and cork pitch. On microscopic examination of the cancer squamous cell epitheliomas were found, the same type that developed in workers in briquet factories and sometimes described as pitch cancer. As preventive measures of importance, the author points out (1) that the formation of pitch dust should be prevented and kept at a minimum, (2) workers with a sensitive skin should not be employed, and

of those who are employed, a rotation of workers is advisable, (3) the workers should be informed about the dangers and of the necessity of protection, (4) cleanliness and change of clothing should be encouraged, (5) a periodical medical examination every 3 or 4 months should be prescribed so that precancerous growths may be recognized early.

The frequency of cancer is greatest among those people with a comparatively high standard of living and is also due to the fact that more than 63 per cent. of cancers affect the digestive organs, pointing to *diet* as an etiological influence as described by E. Grandjean (Schweiz. med. Wchnschr. 60:823 (Aug. 30) 1930). People such as the Hindus and many primitive tribes living on a milk and vegetable diet show much less cancer than the population of countries where the foods provide large quantities of proteins, especially those derived from animals. Grandjean states that the benzene derivatives of intestinal putrefaction resulting from diets rich in animal proteins exert continuous growth stimulation on the healthy cells, and gradually the constantly irritated cells develop into malignant cells. However, the benzene derivatives are formed not only in the intestines, but wherever in suppurative processes disintegration of protein by anerobic bacteria occurs, for example in the lungs, in the female genitalia, in abscesses of the teeth, in alveolar pyorrhea and in ulcers. Benzene derivatives are significant in the etiology of cancer also as shown by the fact that occupational cancers are most frequent in individuals who come in contact with benzene and coal tar products. In order to reduce the frequency of cancer in protein eating individuals, Grandjean states that it is advisable to decrease to a minimum the intake of those

proteins that form benzene derivatives, such as meat, eggs and the plant proteins contained in legumes, such as beans, peas and lentils. The proteins required by the organism should be obtained from milk and milk products, since these cause a bacterial flora that is antagonistic to the bacteria of putrefaction. Also regular defecation is important in the prophylaxis of cancer of the digestive organs.

**Precancerous Lesions.**—In a discussion of the clinical, microscopic and therapeutic considerations of cancer supervision in *skin diseases*, J. J. Eller and N. P. Anderson (J. A. M. A. 94:382 (Feb. 8) 1930) state that the importance of the early recognition of the various types of cancer has always been emphasized. This is due to the fact that the percentage of cures can be raised considerably when malignant tumors are treated radically at their inception. If this is true, it should also be important to recognize the pathologic conditions that might be forerunners of cancer and to eradicate them. There are more than 20 skin conditions which may be the forerunners of cancer:

**Syphilis**—The leukoplakia that occurs on the mucous membranes of mouth, tongue and oral cavity is subject to malignant degeneration. Tertiary manifestations of the mucosa of the mouth and tongue play an important rôle in precipitating carcinomatous growths. The malignant tumor often develops in scars from previous syphilitic ulcerations. It is thought that cancerous growths on a syphilitic base are stimulated to more rapid growth by arsenicals.

**X-ray or Radium.**—Cancer may be caused by a large overdose or too numerous small doses. The prickle-cell cancer is the type invariably found.

**Moles**—Bluish, black or slate moles, which as a rule, are not hairy, are the clinical types apt to develop into melanocarcinomas.

**Senile Keratoses and Seborrheic Keratoses**—Both basal and prickle-cell types of cancer have been described following these conditions. Seborrheic keratoses of the trunk and face are not prone to become malignant.

**Kraurosis Vulvæ**—This condition is complicated with cancer in about one-tenth of the published cases.

**Occupational Keratodermas**—These usually are of prickle-cell type and are preceded by keratoses. "Tar carcinoma" is most frequent in England. Sheep-dip workers may be subject to arsenical cancer, also wallpaper workers, smelters of ores such as tin, nickel, lead, copper, iron and silver. Furriers and tanners are also affected.

**Lupus Vulgaris**—Prickle-cell is the type found. The face lesions are most likely to become malignant. It is more frequent in males, and occurs under 40 years of age. It has been increased by the widespread use of the x-ray.

**Arsenical Keratoses**—Follows cutaneous hyperkeratoses, which are the result of arsenic taken internally.

**Sebaceous Cyst**—Squamous cell epithelioma forms in the cyst wall.

**Lupus Erythematosus**—Is of prickle-cell type. It occurs in areas about the face and scalp, and in long standing lesions.

**Chronic Ulcers and Fistulas.**—Occur but are infrequent.

**Page's Disease of the Nipple**—This is now placed in the class of true cancer.

**Cicatrices.**—These are of the squamous type.

*Cutaneous Horns*—Epithelioma is a frequent complication

*Bowen's Disease*—The lesion may remain indefinitely within the confines of the dermis, or it may break through the basement membranes and become an infiltrating carcinoma

*Extramammary Paget's Disease*—Deeper structures, such as sweat glands, pilosebaceous apparatus or other sub-jacent glands always have a carcinomatous involvement

*Papilloma of the Tongue*—When cancer occurs it is of the squamous type

*Xeroderma Pigmentosum*—Basal-cell cancer is the type usually caused. Treatment is palliative. Keratoses and ulcerations should be removed by electro-coagulation.

*Inflammatory Dermatoses*.—Eczema, lichen planus, and psoriasis occasionally give rise to cancer of the skin, but in the vast majority of the cases reported it is probable that either arsenic or the x-ray was the true cause

In discussing the precancerous lesions of the alimentary tract, M. J. Stewart (Lancet 2 565; 617 (Sept 12, 19, 26) 1931) in the Croonian Lectures states that in the year 1929, there were in England and Wales 56,896 deaths from cancer, in which at least 60 per cent in men and 42 per cent. in women were referable to the alimentary tract. He finds the most hopeful side of cancer research is that concerned with the demonstration of local causative factors and the recognition and prevention of precancerous lesions of one kind or another. This is easily approached for superficial forms of malignancy, but the precancerous lesions of the alimentary tract are not so well outlined, nor are there the same opportunities for prophylaxis

Stewart classifies the chief precancer-

ous lesions or alleged lesions of the various portions of the alimentary tract as follows. (a) Chronic inflammatory lesions (1) leukoplakia, (2) lesions due to burns and chemical caustics; (3) hepatic cirrhosis, (4) hemochromatosis; (5) cholelithiasis and cholecystitis, (6) chronic gastric ulcer; (7) chronic gastritis; (8) chronic duodenal ulcer, (9) diverticulitis (b) Simple tumors as precursors of cancer (c) Lesions due to animal parasites.

*Leukoplakia*—Stewart points out that the squamous epithelial lining of the mouth, pharynx and esophagus, vulva, vagina and vaginal portion of the cervix, as well as part of larynx, is different from the ordinary surface epithelium of the body, since it fails to form a definite stratum corneum, the effete surface cells of the surface being eliminated at an earlier state of their development. In the transitional epithelium of the urinary tract there is no keratinous layer, but even the stratum granulosum or stratum lucidum are lacking. However, in certain conditions of chronic irritation, patches of fully developed highly keratinous epithelium are found in the situations mentioned, and these affected areas are white and opaque, stiff and unyielding, and are liable to become cracked, fissured and ulcerated. The causes of leukoplakia vary according to the site. In the mouth, Stewart holds the chief cause is syphilis and admits that heavy smoking and more or less heavy drinking may have some effect. With leukoplakia of the lip, however, he states that there is little evidence that syphilis is of any consequence in its occurrence. Leukoplakia of the vulva is not a luetic manifestation. It may have some association with cessation of the ovarian function. In the urinary tract, chronic inflammatory



and obstructive lesions are usually found. Redewill points out that vitamin deficiency, especially deficiency of vitamin A, is an important etiological factor, and claims that 2 cases were cured by increasing the vitamin content of the diet, and administering parathyroid extract

The relationship between leukoplakia and carcinoma varies according to the site in the body. In a series of 447 cases of leukoplakia, 130 had already become cancerous, and there was still abundant time for others to develop cancer, due to the youth of some of the patients. The relationship between leukoplakia and carcinoma of the esophagus is very slight, but leukoplakia of the vulva is an extensive precancerous lesion. The relationship between leukoplakia and cervical cancer is not well demonstrated

*Burns and Caustics*—Concerning lesions from burns and other caustics, Stewart (*loc cit*) cites Lane-Clayton who believes that the unglazed clay pipe, especially if broken off, may cause chronic burning of the lower lip to the extent that cancer may develop. Prolonged exposure in the open air is cited by Young and Russell who found in farmers, merchants, seamen, dock-laborers and outdoor railway men cancer of the lip in 200 to 300 per cent greater frequency than would be expected. They compare the findings of coal miners working below ground where smoking is forbidden with those working above ground in not suffering from excess of lip cancer

In 1930, Lane-Clayton demonstrated that in certain districts of India where betel-chewing is a widespread habit, carcinoma of the cheek is very frequent. The betel quid is ordinarily carried inside the cheek and it is on the buccal

mucosa just opposite this point, opposite the molars and premolars, that the changes occur which finally lead to malignancy. Inflammatory thickening and roughening of the mucosa, leukoplakia and epithelial denudation occur and are followed by progressive ulceration

*Cirrhosis of Liver*—In discussing hepatic carcinoma, Stewart describes the liver-cell type or hepatoma, and the bile-duct type or cholangioma first described by Yamagiwa in 1911. The former is much the commoner. Stewart accepts the fact that cirrhosis of the liver is a precancerous condition, finding in statistics figures showing a higher incidence of cirrhosis to cases of primary carcinoma. He states that carcinoma in a cirrhotic liver is the end stage of a well recognized series of pathological changes. Both the portal cirrhosis and the acute cytolytic necrosis are due to the action of toxic substances, some of which are definitely known or suspected, *i e*, trinitrotoluene or alcohol. While sarcoma of the liver is extremely rare, there appears to be a certain relationship with cirrhosis. Jaffe, in 1924, collected and analyzed the available data, finding that of 48 cases of sarcoma, 15, or 29.2 per cent., were accompanied by cirrhosis

*Hemochromatosis*—Hemochromatosis, likewise, when found in the post-mortem room is always accompanied by some degree of hepatic cirrhosis, and Stewart suspects that it may have an association with primary carcinoma of the liver. He describes 3 cases in a series of 13 cases of hemochromatosis

Leitch, in 1924, submitted evidence pointing to gall-stones as capable of causing carcinoma of the gall-bladder. This investigator inserted into the gall-bladder of a series of guinea-pigs human gall-stones, pebbles and pilules

of pitch and lanoline, and in 8 of these, an apparent adenocarcinoma developed in 5½ to 12 months. While the tumors had not undergone metastasis and were not flagrantly malignant, they were definitely infiltrative and had invaded the liver, diaphragm and abdominal muscles. Physical trauma rather than chemical irritation was accepted by Leitch as the original factor of importance.

*Gastric Ulcer*—The relationship between gastric ulcer and malignancy is a topic of perennial interest. Occasionally, although rarely, a simple chronic ulcer and a carcinoma may exist independently in the same stomach, Stewart describing 3 instances in a series of 366 operation specimens noted between January 1, 1921, and June 1, 1931. In 1 case, at autopsy, the lesions were situated side by side and their independence was manifest, since they had come together in consequence of the centrifugal spread of the malignancy. When a carcinoma arises in a chronic ulcer, it does so in the margin, probably at one point only, and then, as the tumor grows, it tends to encircle the ulcer rather than to penetrate the sclerotic floor, meanwhile growing outward. Finally, the crater becomes completely surrounded by the growth, while the floor itself may be partially invaded.

*Polypi*.—The chief precancerous lesions of the large intestines are the benign adenomatous polypi and a subvariety is the familial polyposis. Stewart finds that there is scanty evidence in the human being of any connection between animal parasites and cancer of the alimentary tract. Schistosomiasis, which is the chief cause of the high incidence of carcinoma of the bladder in Egypt, is etiologically unrelated to either carcinoma of the liver or carcinoma of the large bowel.

In concluding his brilliant work, Stewart (*loc. cit*) emphasizes the extraordinary breadth and diversity of the field of cancer research, including the nature, causation, prevention and treatment of the numerous and various precancerous states, a field of almost illimitable scope, and a splendid training-ground alike for pathologists and clinicians.

It is not strictly proper to compare the cancer cell, with its intense egoism, living selfishly at the expense of the organized social group of cells which make up the human body, to that of the anarchist in society, since, as shown by H. E. Robertson (*Colorado Med* 27 4 (Jan) 1930), the anarchist should arouse some opposition, and this, the cancer cell does not do. Within the human organism there is not found any evidence of a defensive or resentful phenomena in the vicinity of a malignant growth. Robertson arrived at this conclusion after studying the *polypoid masses* occurring in the mucosa of the colon. These he found in 50 per cent. of individuals over 30 years of age and, while in the vast majority of cases they never develop into cancer, every one of these polypoid growths shows an unusually large number of characteristics common to cancerous growth. Hyperchromatism, mitotic figures, irregular size and arrangement of cells and general disorderliness of structure may exist to an extent that it is difficult to accept the growth as one of innocence. In those cases where cancerous growths are actually present in the colon together with the polyps, there is no sharp line of differentiation between the benign and the malignant neoplasms. Robertson states that there is an influence exerted on the lining of the bowel which in at least 50 per cent. of adult human beings causes

abnormal proliferation In 1 case this may result in the polyps, in another in a definite cancer Further consideration of the question as to whether a polyp becomes cancerous since it contains late malignant cells in its earlier stages or because of a metaplasia of benign cells, is discussed by L Bonnet and H Bulliard (Ann d'anat path 7 1039, 1930), who reviewed the literature on polyps of the bladder and uterus and report on certain cases personally observed Bladder polyp has been observed by Zuckerkandl, Lubarsch and Steinhaus, who are of the opinion that if a polyp does become malignant, careful examination in its earlier stages would have revealed atypical cells; Guyon, Legueu and Marion, however, believe that cancer develops in benign bladder polyps

The nasal polyps are divided into soft and hard types, the soft ones being common, inflammatory and benign, whereas the hard polyps are relatively rare, only 60 cases being found in the literature by Eckert-Moebius The hard polyps histologically appear benign, but they show a striking tendency to quick recurrence after excision, and toward metaplasia of their cylindrical cells to squamous cells, or even into epithelial pearls These authors describe a soft nasal polyp, at the periphery of which was an inflammation, but at the base it was branching, typically papillomatous, and benign

The second nasal polyp showed a benign papillary structure as a whole, but its fibrous axes were thin and its epithelium appeared in many layers The surface cells were squamous and here and there were cornified. In the deeper layers the cells showed transitions between ciliated and squamous cells Some of the epithelial cells showed irregular and multiple nuclei, and some were nucleated like giant cells Mitoses were

moderately numerous. This lesion was regarded as precancerous

The third specimen was similar to the second, with cords and deep bays of cells invading the tissues The epithelial cells showed large acidophilic nuclei The stroma appeared to be filled with plasmocytes and Russell bodies, and numerous mitoses were present

The uterine polyp studied by these observers revealed certain signs of malignancy It was an example of a mucous polyp and was bordered by inflamed connective tissue and plaques of epithelium The stroma was infiltrated with round cells and was edematous and very vascular There was marked proliferation of the covering epithelium about a gland the lumen of which was still apparent, but the mucous cells of which were limited to the region near the lumen or were absent altogether Within the epithelial invasion, pearl-like structures and numerous mitoses were seen The epithelium was largely squamous

Bonnet and Bulliard (*loc cit*) are of the opinion that malignant degeneration from these polyps is due to metaplasia of the cells rather than to the presence of malignant cells from the beginning They also state that malignancy in polyps is not exceptional, but bladder polyps, which often become malignant, should be in a class by themselves

**PATHOLOGY.**—F. Voltz (Arch f. Gynak. 143.1 (Oct. 24) 1930) divides cancers into 4 groups (1) *Type A*, has a highly favorable course from the time treatment is instituted, (2) *type B*, which is at first favorably influenced by treatment but later becomes refractory, (3) *type C*, which from the beginning is refractory, and (4) *type D*, which at first appears refractory to treatment, but later is favor-

ably influenced. In *type A*, both the correct treatment was chosen and optimal conditions for cure were apparently present. In *type B*, the author urges an attempt should be made in each case to determine why the transient cure was followed by a recurrence. He states that in some cases this may be explained by incorrect technic or insufficiency of treatment, or by predisposition to recurrence. This is likewise the case for *type C*, in which the course is unfavorable from the beginning. In these patients the principal interest is found in a predisposition for the complete failure of the treatment used. For *type D*, the treatment advised, the extent of the cancer, and its microscopic characteristics are to be more detailed in study.

G. W. Crile (Am J Surg 12 213 (May) 1931) describes researches in the formation of autotrophic cells, with special reference to fertilization, the growth and production of cancer cells, and the etiology of fatty degeneration. In his laboratory, the lipoids and proteins of the brain of freshly killed normal animals were extracted and reduced to ash. Then, by mixing together the brain lipoids, proteins and a solution of the brain ash, or of the electrolytes found in the brain, the process of fertilization in nature by the union of the spermatozoon and ovum was roughly imitated. Cell-like forms were observed which multiplied sometimes by budding and sometimes by direct division. Crile found these autotrophic cells to be nucleated and that they absorbed intravital stains, consumed oxygen, gave off carbon dioxide and produced urea. The control experiments pointed to the fact that the brain lipid was unique in collaborating with electrolytes and organizing the proteins of any organ. When the brains of dogs dying from distem-

per were used for material, the autotrophic cells were not formed, nor would they form in a rabbit which had died from exhaustion due to insomnia.

Crile finds an importance in his work with special reference to cancer formation and the presence of changes in the hydrogen-ion concentration. He maintains that continued alteration in the pH may be a strong factor in reducing the highly differentiated molecules of the normal cells to a lower level—that of growth only—or, in other words, to the cancer level. Crile disbelieves that cancer cells have a higher dynamic potency than ordinary tissue cells, and he suggests that the success of cancer in the body is due to unpreparedness for gross competition on the part of the tissues and organs, rather than to the severity of the attack of the cancer cells.

It is still generally held that sarcoma spreads by way of the blood stream and carcinoma chiefly by the lymphatics. A true differentiation, however, on this basis does not exist, according to H. Baumecker (Deutsche Ztschr f. Chir 221 12 (Nov) 1929). Surgeons find changes in lymph glands with a certain regularity. Frequently these glands show chronic lymphadenitis with desquamated, proliferated and enlarged sinus endothelial cells.

Baumecker found no infection of the tumors observed in his clinic, and he states that these changes in the lymph glands are a manifestation of metabolic rather than inflammatory processes. He came to the significant conclusion that the endothelial proliferation is due chiefly to metabolic products given off by the primary tumor. Occasionally, swollen cells are cast off and may be free in the sinuses, where they are erroneously interpreted as being invading carcinoma cells.

While it cannot be denied that the tumor cells may be carried to regional lymph glands through the lymphatics, Baumecker (*loc cit*) cannot understand how these displaced cells can multiply to such an extent and reproduce organic structures resembling the tissue of origin. This observer finds in tumor metastasis an expression of a general metabolic disturbance manifested in tumor cachexia rather than as a condition of local origin. To prove this point, he cites experiments in which, under the influence of chemical substances, as tar, distant effects in the form of tumor growths appeared in other regions rather than at the site of inoculation. The initiating factor remains the unknown factor that provided the original impulse for tumor formation. The development of cancer in the lymph glands is intimately associated with the reticulo-endothelial system.

Histogenetically, primary cancer of the lung has been described in 3 different groups, according to the epithelial unit which the lungs have been interpreted as containing, which B. M. Fried (Medicine 10: 373 (Dec.) 1931) enumerates as follows: (1) The epithelium lining the bronchi, (2) epithelial cells which form the mucous glands, and (3) the epithelium said to line the pulmonary alveoli or air sacs. From the microscopic standpoint, this classification was accepted (1) on the type of cells said to resemble those of the matrix, (2) on their arrangement, and (3) on some properties of the cells such as secretion of mucus.

Fried (*loc cit.*) does not agree entirely with this method of classification and states that it cannot be relied on, since those who have studied primary pulmonary carcinoma have noted the protean clinical manifestations of the

malignant disease. He states that the microscopic features of a fully developed pulmonary tumor point to its histogenesis only in exceptional instances, and that the morphology of the neoplastic cells varies from one tumor to another, as for example, the columnar, cuboidal, spindle-shaped, squamous epithelial cells or basal cells, and even in the same tumor their cells frequently vary from area to area.

Fried states that from postmortem material a large percentage of all pulmonary tumors are of the basal or squamous cell types, and since cells of this type are normally not found in the lungs, the origin of these tumors is said to be due to metaplasia of the ciliated columnar cells. The conception of a direct transformation of one well-characterized tissue into another was originally advanced by Virchow, but such a hypothesis, in Fried's opinion, is not borne out by close observation. Fried cites Wells, who, in 1925, stated that formation of metaplastic squamous epithelium brings to mind 2 puzzling topics, one of a chemical and the other of an embryologic nature. Chemically, squamous epithelium is characterized by the formation of keratin, which is a definite chemical compound formed, as a rule, by cells of ectodermal origin. When cells of endodermal origin assume the function of forming a peculiar protective chemical substance, they have taken on a chemical function far removed from the normal ability.

Pathologically, there is another problem. When the cells assume the proliferative activity characteristic of malignant disease, they usually lose their more recently acquired functions and maintain chiefly the simple vegetative function of proliferation. When a transitional or columnar epithelial surface be-

comes squamous by metaplasia, and the same protracted irritation that caused metaplasia continues until cancer is formed, Wells finds that the newly acquired property of forming keratin has become fixed, and the cancer is a keratinizing, squamous cell carcinoma.

Fried (*loc cit*) states that carcinoma arising primarily in the lungs is bronchiogenic, and that it is due to excessive regeneration following chronic irritation of the bronchial system. Only the basal cells are concerned in a process of regeneration of bronchial mucous membrane, and, therefore, these cells serve as a sole matrix for primary bronchiogenic carcinoma. Furthermore, primary squamous cell epitheliomas and basal cell epitheliomas of the lungs do not result from metaplasia of the pre-existing ciliated columnar epithelium, but arise through protoplasia or indirect metaplasia of the undifferentiated basal cell of the bronchial mucous membrane.

**DIAGNOSIS.**—In recent years there has been no new method of diagnosis applicable to all forms of malignant disease, as pointed out by C. F. Geschickter (J. A. M. A. 94:326 (Feb. 1) 1930). Numerous individuals, as Fry in London, Carminati in Milano and Auler in Berlin, are endeavoring to devise some means of serum diagnosis, but as yet no reliable results have been obtained. Biopsy and the use of the frozen section method for tumor diagnosis is not utilized as frequently in Europe as in America. At the Johns Hopkins Hospital and at the Cancer Hospital in London, searchers are endeavoring to find a differential cancer stain which will make frozen section diagnosis more accurate and useful.

Lipschutz, of Vienna, states that he has demonstrated a specific morphology in the cancer cell, using a new method

of staining tissue with a Giemsa dye. By the use of this dye, he shows a semi-circle of basophilic granules outside the nucleus of the tumor cell which he designates as a "plastin reaction." The results shown by Lipschutz, however, are not applicable to frozen sections or to practical diagnosis and have, therefore, not been extensively utilized.

All of these endeavors to find a new diagnostic procedure must be guided by reliable and definite standards for the recognition of this disease. In borderline cases, at the present time, as pointed out by Geschickter, the only standard is the combination of the microscope with the clinic follow-up data. The latter is, of course, cumbersome and entails a long time. On this account, refinement in microscopy to the point of certainty in tissue diagnosis is most desirable, and the chief hope in this direction at present is a reliable differential stain for cancer.

A. Epstein and Fedorejeff (Arch. f. klin. Chir. 165:357 (May 15) 1931) state that occasionally reports concerning injurious results of biopsies for diagnosis of malignant tumors are found in the literature. Such complications as infection, hemorrhage, or stimulation of the tumor growth have been mentioned, but no report shows the percentage of these cases to the total number of biopsies. The authors, therefore, examined a large number of patients in whom biopsy had been performed at the Oncologic Institute in Leningrad and also reviewed the literature. Their conclusions are as follows: (1) complications following carefully performed biopsies are rare; (2) sarcomas usually react with accelerated growth more frequently than cancers; (3) to avoid any complications following biopsies a radical operation, electrocoagulation or



chemical cauterization should follow immediately. Irradiation may be begun before the biopsy, and, following it, should be either resumed immediately or discontinued, (4) in cases of non-ulcerated tumors that are covered with normal skin, regional lymph glands that appear to be involved should be completely removed; (5) if these lymph glands are not present, or in cases of mucous membrane, the biopsy should be done with the diathermy loop; (6) in tumors of the mammary gland, biopsy as an independent intervention should be avoided. As the first step in intervention, it may, however, be permissible, and in these cases the biopsy specimen should be immediately examined by means of the freezing microtome and after that the breast, if necessary, may be amputated, (7) tumors in the form of small nodules on the tongue, lips, etc., should be removed totally within healthy tissues.

W. M. Wright and C. G. L. Wolf (J. Cancer Research 14:370 (Aug) 1930) review the work which led to the discovery of the *Fuchs serological test* for the diagnosis of malignancy. They made 116 determinations in malignant and nonmalignant patients. They found that if serum from a patient suffering from cancer is permitted to stand in contact with washed blood fibrin from a normal person, it causes proteolytic splitting of the fibrin, which is manifested by an increase in the nitrogen content of the filtrate from the mixture. Normal fibrin is carefully separated, washed, ground and put in a 5 mgm sterile tube. To 1 tube of this is added 1 c.c. of suspected cancer serum and incubated for 24 hours, then trichloroacetic acid is added, the mixture is filtered and the nonprotein nitrogen in the filtrate determined by the micro-Kjeldahl

method. With cancer serum, a definite increase 4 to 5 times the control in non-protein nitrogen is observed.

The rationale of the test is observed as follows. The Abderhalden test in the diagnosis of pregnancy depends upon the detection in the blood serum of certain substances causing increased proteolysis, as shown by tests for products of protein splitting. A loose analogy between the formation of placenta and the development of malignant growths suggested to several investigators that the blood of cancerous patients might show similar changes. A precipitin reaction with cancer and placenta extracts reacting with a corresponding sera had been obtained, using antiserum for specific organisms obtained by immunization.

Abderhalden was of the opinion that normal serum contains no ferment capable of splitting protein, but when Stephan and Wohl, using animal fibrin, noted proteolysis, Fuchs reasoned that proteolysis takes place when the fibrin is from another animal (heterologous), while sera and fibrin from the same (homologous) animal causes no proteolysis. Using cancer patients, he found proteolysis when cancer serum was mixed with fibrin from a normal blood or cancer fibrin when mixed with normal serum, but no reaction was obtained when the serum and fibrin came from the same patient. Of the 116 examinations made by Wright and Wolf (*loc cit*), no case diagnosed clinically as malignant gave a negative reaction, but a positive reaction in about 25 per cent. was given by miscellaneous conditions such as hemorrhoids, chronic appendicitis, and enlarged prostate. Some of the patients gave a positive reaction before treatment and negative reactions after the use of radium.

In 124 cases diagnosed as cancer, J Adams-Ray (*Acta chir Scandinav* 66 263 (May 30) 1930) studied the *sedimentation reaction* at the end of an hour and found that normal and slightly pathologic values did not exclude cancer, this being especially true in tumors of the breast. Medium high, high, and very high values should awaken a suspicion of the presence of cancer, which increases with the rise in the value of the sedimentation reaction. Of cases with visceral metastases, 25.7 per cent fell within the group "normal and slightly pathologic values"; 53.3 per cent of the operable cases gave medium high and high values; and 84.4 per cent of the inoperable cases and of those with visceral metastases, showed medium high, high and very high values. The latter values, however, were obtained only in the inoperable cases (15.8 per cent). Among the ventricular carcinomas, 9 cases with the Weber reaction under 25 mm. were noted, but of these, only 4 were operable, while 2 were technically inoperable and 3 had viscera metastases. Adams-Ray, therefore, believes that the sedimentation reaction does not give a reliable basis for judging operability, except when the value is high, when it is a case of inoperable tumor.

*Mitogenetic radiation* as a method for early diagnosis of cancer was first described by L. D. Gurvitch, in 1925, who showed that the process of blood radiation is based on oxidation which depends on the action of oxyhemoglobin. This investigator (*Vrach gaz.* 35:15 (Jan 15) 1931) has demonstrated that substances which were oxidized and produced the mitogenetic effect are the polypeptides and also likely the amino-acids contained in the blood serum. The reaction of the blood of mammals and

that of frogs and birds is different. The oxidation process of mammals' blood is not the main and sole source of radiation. In the method described by Gurvitch, he used yeast cultures as a detector. The first series of experiments performed on mice inoculated with adenocarcinoma showed identical results, the blood radiation disappearing in all inoculated mice. These same findings were noted in 17 persons with various cancerous conditions. All of the healthy individuals examined with other diseases gave a positive mitogenetic effect. Patients with diseases of the blood, as pernicious anemia, leukemia, septicemia, pyemia and gangrene, gave a weak radiation or none at all. The author states that the mitogenetic radiation in cancer patients is typical but is not specific.

Four cases of *disseminated carcinomatosis* of the skin are described by P. Uhlenbruck and E. Gilardone (*Med Klin* 26:627 (Apr. 25) 1930), who are convinced, following the study of these cases, that cancer nodules beneath the abdominal skin are usually lymphogenic metastases of abdominal tumors, whereas hematogenic isolated metastases on the chest, abdomen or back are frequently the beginning stage of disseminated carcinomatosis.

**PROGNOSIS.—Gynecologic Cancer.**—Taylor (*Am. Jour. Cancer* 15 2517 (Oct) 1931) presents a clinical and pathologic study of 739 cases of gynecologic cancer observed at the Roosevelt Hospital from 1910 through 1930. *Cancer of the cervix*, in the only 2 reportable years (1924-1925) in which radium was used practically exclusively, was curable for at least 5 years in 18 per cent of all cases. The amount of irradiation in these years was inadequate. An increase in dosage,

a better method of application, and the addition of high voltage x-ray therapy will, it is hoped, lead to improved results for the years after 1927. In the years 1921-1923, however, when the plan of treatment for favorable cases consisted of preoperative radium and later radical hysterectomy, the absolute 5-year cure rate was 29.7 per cent.

*Carcinoma of the corpus* gave an absolute cure rate of 25.8 per cent, a disappointing figure, owing in part to a large number of lost cases. Among the traced cases in which operation was performed the results approached the average reported by other institutions. The high mortality, especially in women over 60, leads to the suggestion that irradiation should be substituted for surgery at least in this group.

*Carcinoma of the ovary* yielded only 6.9 per cent of cures, a very low figure, owing perhaps entirely to a review of the sections and the exclusion of all cures in cases possibly classifiable as papillary cystadenoma. The successes were all due to factors uncontrollable by the surgeon, *viz*, the restriction of the growth at the time of operation to an unruptured cyst. X-ray therapy has not produced cures in otherwise incurable cases in the Roosevelt clinic but will be continued in view of favorable outside reports.

*Carcinoma of the vulva* yielded 21.1 per cent of cures, but it is probable that this figure might have been larger had several of the patients in the early cases not been at first treated by a too conservative operation.

*Carcinoma of the vagina* has recently been treated by radium, which has led to some preliminary encouraging results.

*Sarcomas of the uterus and ovary* offer difficulties in histologic diagnosis which may largely affect the reported

percentage of cures. From a more practical point of view a failure on the part of either surgeon or pathologist to differentiate myosarcoma from a benign fibromyoma may jeopardize the individual patient's chances.

A few rarer tumors, *carcinoma of the tube*, *chorioneptelioma*, and *sarcoma of the rectovaginal septum* are reported. An apparent cure is noted in a case of the disease last cited.

Advanced *peritoneal malignant tumors* of undetermined origin, usually regarded as ovarian, are separately considered. They form a fairly large and quite hopeless group.

A careful review of the pathologic sections of cases of cancer of the cervix has led to little corroboration of the finding of several writers that histologic form bears a relation to prognosis as the result of variations in malignancy or in radiosensitivity. There was a very slight indication of such a relationship in carcinoma of the corpus. The correct separation of corpus adenocarcinoma from endometrial hyperplasia, of papillary cystadenocarcinoma of the ovary from papillary cystadenoma, of myosarcoma from fibromyoma, and of fibrosarcoma from fibroma of the ovary is, however, of vital importance in prognosis.

**PROPHYLAXIS AND TREATMENT.**—J. C. Bloodgood (Am. J. Cancer 15:1577 (July) 1931) states that at present the principal hope of increasing cancer cure rests on increasing the power of the x-ray tube, and he furthermore states, that the value of public education, and also of the medical profession concerning earlier and more accurate diagnosis, of more skilled operative procedures and radiotherapy, should be well known. Bloodgood is of the opinion that cancer cannot be

completely eradicated by periodic examinations or by annual pelvic examinations of women, such as may be used for examination of lesions of the skin, mouth and other more external and superficial regions. Bloodgood believes that the final eradication of cancer will depend on the development of some kind of **intravenous therapy**, or on the discovery of the cause of cancer which may point to a specific or curative treatment.

G de Caetani (Tumori 5 477 (Sept-Oct.) 1931) has studied in 2 groups of researches the result of **histochemotherapy** in malignant disease, and also the results of attempts at prevention with **extracts of stimulated antitlastic goat organs**. In the first series of experiments de Caetani used rats in which a fusicellular sarcoma or adenocarcinoma was present, and these animals were treated with an organotherapeutic preparation. The experimentalists observed constant retrogression of the tumor mass, as shown histologically, which was similar to those findings noted in homogenous resistant and in heterologous nonreceptive animals. In a second series of experiments de Caetani then tried to develop in rats a state of nonsusceptibility to the "taking" of the tumor after its development following inoculation. The author used injections of extracts of stimulated antitlastic organs and was able to produce a condition which almost always prevented the taking and the further development of the tumor following inoculation. He then discusses the possible approach in studying cancer in man by using organotherapy.

**Treatment.**—A S Warthin (Ann Int. Med 4 398 (Oct.) 1930) states that the newest field of cancer therapy investigation is based upon the effort to

influence the metabolism of the cancer cell and describes the experiments of Warburg on mice who aimed at starving out the cancer cells by interfering with their sugar and oxygen supply. The experimental animals were made to breathe an atmosphere containing only 5 per cent of oxygen over a period of several hours. Probably because of the overcrowding of the cancer cells and through injury to the cells of the thin-walled blood vessels of the neoplasm, the tumors were less resistant to oxygen lack than the normal tissues and biopsies proved that practically all of the cancer cells died or ceased to function. Attempts to alter the sugar supply of the tumors by maintaining the experimental animals in insulin shock did not seem to influence the tumor growth. Other similar experiments to date have been fruitless.

Fischer-Wasels, of the Senckenberg Pathological Institute in Germany, has presented the latest new method of cancer therapy on the theory of influencing the general metabolism of the body and that of the cancer cells in particular, based on Warburg's theory of the pathological respiration of tumor cells, as well as upon the alkalosis of the blood seen in cancer patients by Reding and others. Basing his suggestions and procedure upon animal experimentation, Fischer-Wasels has used the following treatment for cancer in the human subjects for the past 1½ years.

**A Local Treatment.**—Intense deep x-ray therapy of the primary tumor and of metastases, when present, after the method of Holfelder.

**B. General Treatment.**—1. Daily 2 to 4 hours breathing of a mixture of pure oxygen and 5 per cent. carbolic acid, with tightly fitting mask to avoid apparent respiration.

2 Three times daily, following meals, **hydrochloric acid** by mouth in the largest possible doses. He gives this for the control of the acidity of the urine.

3 Activation of the reticulo-endothelial system by **ultraviolet irradiation** (Alpine sun) of the entire body, the dose being regulated according to the individual. In order to prevent overloading of the reticulo-endothelial system, the ultraviolet irradiation should never be carried out on the same day as the x-ray irradiation.

The treatment must be carried along over a period of many months without interruption, and, therefore, is very expensive owing to the cost of the gas-mixture. A number of cases of *carcinoma of the esophagus*, *inoperable carcinoma of the stomach* and in a case of *carcinoma of the mammary gland* with generalized metastases, good results are claimed. Less successful were those cases of *cancer of the cervix*, *uterus* and *intestine* treated with this method. The treatment, however, seems to have good effects on the ability to sleep, appetite, blood and on the body weight.

Certain cases of cancer appeared to have been favorably influenced by the method of treatment employed by S. M. Copeman (Brit M J 1 658 (Apr 18) 1931). Some of these cases were regarded as inoperable. This treatment consists of using a slightly **alkaline solution of the sodium salt of fluorescein** sprayed or painted widely over the surface of the growth and followed by the application of **radium** or a dosage of **x-rays** of moderate penetration. Sometimes the superficial use of fluorescein may suffice for the required purpose, but if the growths are more deeply seated or disseminated, the fluorescein is

also given orally or intravenously. Because of its low toxicity, the fluorescein salt may be given in considerable quantities in one or other of the ways mentioned. An ordinary dose by mouth consists of 2 capsules of 0.5 Gm ( $7\frac{1}{2}$  grains) each. Fluorescein is given internally to bring under its influence, on irradiation, outlying cells that may have become affected, or an organ such as the liver, which may be suspected of having secondary deposits, although no clinical evidence may be apparent. Recently, however, there is reason to hope that by giving the fluorescein internally, as well as by the local applications to the skin, together with appropriate distribution of the subsequent irradiation, the technic may prove successful in preventing recurrence, not only locally, but generally throughout the entire body. When used by the intravenous route, 20 c.c. (5 drams) of a sterilized 5 per cent solution of **sodium fluorescein** should be slowly injected. *Cancer of the breast* seems to respond, whether primary or recurrent, to this treatment.

**Bismuth** has been found by H. Kahn (Deutsche med Wchnschr 56 2131 (Dec 12) 1930) to be the only heavy metal that is deposited selectively in the tumor cells. From this finding, Kahn states that the therapeutic doses of most heavy metals are almost always toxic, whereas in the case of bismuth, the therapeutic effects can be obtained with doses that do not cause toxic effects. He finds that injections of bismuth influence the growth of tumors, even when the injections are combined with irradiation. This author recommends further studies of the radioactive bismuth or radium E in the treatment of cancer.

C. Regaud (Acta radiol. 11 455, 1930) states that there is a radiophysi-

ology common to normal and cancer tissues in man, which appears to be in contrast to that of vegetable cells, bacteria and the ova of lower animals. He mentions that **irradiation** acts in 2 ways on tissues, *i e*, (1) by exerting a direct effect on the more sensitive cells, (2) by exerting an effect on the vasculoconnective tissues which nourish these cells. The first is of value in the treatment of malignant tumors and the second useful in the treatment of chronic inflammations and as a palliative treatment of cancer.

The radiosensitivity of both normal and cancerous tissues depends upon the multiplication of the mother cells. Ideal radiotherapy of cancer uses the favorable interval between the radiosensitivity of the cancer cells and that of the normal tissues. When irradiation extends beyond the margins of serious lesions of the connective tissues and vessels, early or late necrosis may occur.

No single dosage of radiation is curative for all carcinomata or sarcomata, and the variations of radiosensitivity depend upon the histophysiological characteristics of the tumors. Time is an important factor in radiosensitivity. When the treatment is divided and spread out, the therapeutic interval of radiosensitivity decreases, whereas, when the treatment is given over a period of moderate length, the therapeutic interval is increased. This has been shown by experiments on the testicle of the rabbit.

In the Radium Institute of Paris, since 1920 there has been a tendency to prolong the time of treatment both in **x-ray therapy**, as Coutard's procedure, and in **radium therapy**, and the results have shown a decrease in the local and general reaction and general improvement in the effect of the treatment.

Radiophysiology shows that there are

many gradations between entirely elective radiotherapy and diffusely caustic radiotherapy followed by radionecrosis.

R. B. Greenough (Trans. College of Physicians of Philadelphia, Third Series, 51: 245, 1929) considers that the surgeon should play the leading part in the team-work between the surgeon, radiologist, pathologist, physician and specialist, in caring for cancer cases. He maintains that the radical operation, removing in 1 piece the whole of the local disease, together with the structure first in line of extension, offers the best chance for permanent cure. Greenough discusses *cancer of the breast* as the best example, and finds that as high as 50 per cent cures can be obtained in a 5-year follow-up series in which axillary lymph glands are free from infection. A radical operation which fails to achieve complete removal is a mistake. Precancerous operations, as the *keratosis* and *papillomas* in elderly people, are best treated by **radium**, but when any doubt exists, especially if the lesion is of the lip or tongue, where metastases are likely to develop, operation and pathological examination provide information most important for the further observation of the patient.

Greenough points out that, as a rule, the rapidly growing, undifferentiated tumors are the most radio-sensitive, but numerous exceptions to this rule are known. Rodent ulcers, embryomas of the testis, parotid tumors, the lympho-epithelioma of Regaud, and the endothelial myeloma of Ewing are highly radio-sensitive. However, squamous-celled carcinoma and fibrosarcoma are very insensitive to irradiation. Surgery and irradiation supplement each other in many ways.

Surgery, x-ray and radium irradiation are but local therapeutic attacks on can-



cer growths, as pointed out by H Rubens-Duval (Bull et mém Soc d Chir de Paris 23 310 (May 15) 1931) and these agencies act only locally and not on the reaction of the organism as a whole. **Specific protein therapy**, however, exerts an effect on the entire body. Rubens-Duval has prescribed a specific globulin by mouth, no matter where the tumors may be located, and finds that this form of treatment controls and modifies the evolution of the cancer cells through the reaction of the organism as a whole, acting as a complement to surgery. The author describes 3 cases of inoperable cancer in which protein therapy was given before operation, and in 2, following operation. The first patient, a woman of 37, had a *tumor* of the right *breast* with numerous metastases in the axilla. This investigator prescribed daily doses by mouth of 1 cc (16 minims) of a 10 20 dilution of globulins obtained from several epitheliomata of the breast, and a few days later the tumor appeared to be more localized and mobile, amputation of the breast was then performed.

The second case was a woman aged 61, who had a cylindrical-celled *carcinoma of the rectum* confirmed by biopsy. Since the general condition was not favorable, an artificial anus was made on the left side. A small quantity of an extract made from the rectal tumor was then given in a 10:20 dilution. The tumor developed a pedicle and 2 weeks later was surgically removed under local anesthesia. The surgeon, Lawrence, stated that without the general treatment it would have been impossible to operate on the tumor locally. A year following the operation, the patient was in excellent condition, there were no local rectal findings, and the artificial anus was closed.

The third case, a woman of 41, had a recurrence in the scar of a breast amputation performed 5 months before. This patient was given by mouth first a 10 20 dilution and then a 10 21 dilution of globulins and albumoses from *carcinoma of the breast*. The treatment was marked by general fatigue and loss of appetite. The nodules diminished somewhat, and a large subcutaneous mass with a cartilaginous consistency developed which appeared to be operable. In January, 1930, a better preparation of purified globulins was given, and following this treatment, the pains ceased, the patient appeared better, regained her appetite, and the tumor nodules became still more cartilaginous. They were then removed by surgery. Histologically the specimen was an epithelioma with a marked defense reaction, fibrosis, a tendency toward encapsulation and retrogression.

The fourth case is that of a radiologist who had developed an *epithelioma of the right hand* following a chronic radiodermatitis. Electrocoagulation having been followed by recurrence, amputation of the 3 middle fingers of the right hand was performed. Following this, a recurrence developed at 2 points. The patient was then given orally 6 ampoules of a vaccine from the tumor. Two months later he felt better and the local ulcerations had healed. One of the local nodules which was removed surgically showed merely scar tissue and an inflammatory reaction.

The fifth case was a woman aged 38, who had an amputation of the right breast. Three years later she developed a *lymph-gland metastasis* for which she was operated. After this she was given an autogenous vaccine of *cancer of the breast* in a 10 20 dilution. Her general condition remained excellent, but a year

later she had a recurrence the size of a bean in the axillary scar. She was then given the diluted autogenous vaccine in wine and, 2 days later, the recurrence in the axillary scar was removed surgically. It showed a lymphoid reaction and sclerosis about the epithelioma cells.

There appears to be a state of equilibrium between the organism and the cancer cells and just as a benign tumor may become malignant, a malignant tumor may become benign. The process is reversible, and this was shown in tar cancers of rabbits but not in human beings. In cases treated with specific proteins, metastases are rare or delayed. Whenever possible, an autogenous vaccine should be made from the particular tumor present. *Carcinoma of the stomach* and of the *ovary* are perhaps most sensitive to **protein therapy**.

The adult, highly differentiated, radio-resistant tumors, constitute a large number of the neoplasms unsuitable for radiation, and G. A. Wyeth (Radiology 17.1028 (Nov) 1931) considers that these cases are particularly suitable for treatment by **electrosurgery**. Extensive disease and infection are 2 other factors which limit the effectiveness of radiation, and electrosurgery minimizes the importance of both of these factors. Electrosurgery does everything that the scalpel does, whenever it is necessary to remove tumor tissue, with the added protection of sterilized tissues and sealed lymphatics. By means of the cutting-current biopsy electrode and the rapid frozen section method the radio-sensitivity or the radioresistance of a tumor can be determined, in most cases, before treatment is begun. Thus it is possible to avoid the too frequent mistake of excising radiosensitive tumors by the scalpel and overtreating

radio-resistant lesions with persistent radiation.

Among the 85 cases of carcinoma treated by **radium** by H. S. Souttar (Brit. M. J. 2 273 (Aug 23) 1930) there were 11 skin cases in which the tumor disappeared in all, with no recurrence after periods up to 17 months. In all the *lip* cases there was a rapid local response, 3 of the 5 patients remaining well for 6, 13 and 15 months. The 1 fatal case was untreatable when first seen. The *tongue* cases were all advanced and untreatable by any other method. In every instance, however, there was a rapid local response, with, in all but 1, a total disappearance of the primary tumor. In the 4 cases in which the glands were treated by radium, they responded immediately. In 5 of the 7 cases distant secondary deposits appeared, and in only 1 was there any possibility of a permanent cure. This also was, however, a totally inoperable case. The 6 *mouth* cases were all entirely inoperable, 5 of a very advanced and extensive nature. In the only case in which the growth was limited, although surgically inoperable, there has been no recurrence after 2 years. In 4 of the other cases the local growth disappeared but recurred later. Twenty-four *breast* cases are classed as early, advanced and operable, and inoperable. Of the 11 patients in the first group, all but 1 have been followed to date, and these all remain free from recurrence at periods of from 6 to 12 months. The 26 cases of carcinoma of the *esophagus* show that in many cases swallowing can be achieved by means of radium, giving relief for periods up to 14 months.

**CARBOHYDRATE.**—Exhaustive studies of the action of the various carbohydrates on the intestinal peristalsis

and ventricular functioning of guinea-pigs have been made by W. Catel (*Jahrb. f. Kinderh.* 130.305 (Feb) 1931). In all cases lactose, dextrose, levulose, brown sugar, saccharose and Soxhlet's nutrient sugar were used. The reaction to the several carbohydrates, when applied to the intestine, seemed to be identical; as regards the small intestine, the action of the carbohydrate was a specific pharmacologic one. Diarrhea occurring after oral administration of carbohydrate is thought to be caused not by the sugar, but by volatile fatty acids developed on bacterial decomposition of the sugar. In all cases, intestinal peristalsis was impaired from 10 to 88 per cent by carbohydrate in a 1 to 6 per cent solution. Other experiments done by the same author on the hearts of frogs showed that, in most cases, during the summer months the solution produced a positive inotropic action, but a ventricular arrest in systole was never observed. However, the same test performed in winter months showed a negative chronotropic or a negative inotropic action, resulting in the ventricular arrest in diastole. These seasonal differences are thought to be due to changes in the metabolism during the period of hibernation. It is believed that the carbohydrate, through an action on the sympathetic nervous system, causes the impairment of intestinal peristalsis. This author is now attempting to ascertain whether or not the action of the carbohydrate is the result of irritation of the sympathetic or inhibition of the vagus nerves.

**CARBON DIOXIDE.**—Carbon dioxide metabolism in the body has been studied with considerable interest recently. K. Hinsberg (*Klin. Wchnschr.* 9:156 (Jan. 25) 1930) has shown

that patients with disturbances of the circulation require a greater amount of oxygen than normal subjects for the same exertion. It was noted that carbon dioxide baths exert a favorable influence on the general condition of patients with circulatory diseases and Hinsberg reasoned that a patient receiving carbon dioxide baths should consume less oxygen during exercise than one not being so treated. To his surprise he found that there was no decrease in the oxygen requirements, but rather an increase. He also observed that the basal metabolic rate was not markedly influenced by carbon dioxide baths, but when digitalis was administered during the time the patient was receiving the baths, metabolism during work was facilitated. However, he concluded that although this would seem to contraindicate their use, carbon dioxide baths do have a definitely advantageous influence in the treatment of patients suffering with circulatory disorders.

R. J. S. McDowall (*Edinburgh M. J.* 37:463 (Aug.) 1930) considered the use of carbon dioxide baths in an attempt to reduce body temperature and hyperpyrexia. It is a well-known fact that the carbon dioxide of the body is a definite factor in the defenses against invasion of bacteria. He decided that antipyretics were far less satisfactory in reducing high temperature than simple cool baths and that the latter have an added advantage in that the excessive respiration produced by the high temperature is decreased and the body retains the carbon dioxide which is such an important factor in its defense action against the invasion of bacteria.

In studying their effect on the circulation, C. Kroetz (*Ztschr. f. Kreislauforsch.* 22:641 (Oct. 1) 1930) decided that carbon dioxide inhalations are in-

licated in shock and collapse and in chronic vasomotor weakness. The circulatory action is manifested by an increase in the oxygen content of the arterial blood, and an increase in the venous reflux and in the minute volume and beat volume. He feels, however, that carbon dioxide inhalations are contraindicated in definite decompensation of the heart and in angina pectoris.

K. Gollwitzer-Meier and H. Bohn (Klin Wchnschr 9:872 (May 10) 1930), in a study of the effect of carbon dioxide on the venous system, concluded that an increase in the carbon dioxide tension in the blood causes venoconstriction. The venoconstriction is caused by nervous action by way of the vasomotor nerves and does not appear when the nervous connections have been severed.

The use of carbon dioxide during or after anesthesia has been discussed at length by H. J. von Brandis and H. Killian (Deutsche Ztschr. f. Chir. 233: 97 (Oct. 2) 1931) and they conclude that it should be administered in a 5 per cent mixture if it is to be given for a considerable length of time. In the regulation of anesthesia and the treatment with carbon dioxide, the object is to amplify the respiration by producing deep full breathing and at the same time avoiding overexertion of the patient. Should strong stimulation be desired, a few breaths of a highly concentrated mixture of carbon dioxide is effective, but will produce sharp, gasping, deep breaths and cause fatigue if continued for long.

**CARBON TETRACHLORIDE POISONING.**—A. Henggeler (Schweiz med Wchnschr. 61:223 (Mar. 7) 1931) reports a case of carbon tetrachloride poisoning in a school

janitor who developed the symptoms while polishing floors with a floor-wax heated in a hot water bath before application. Inhalation of the vapors caused serious intoxication, followed by a marked loss of weight and, at the end of 22 days, signs of collapse which were overcome only by the use of cardiac stimulants. At one time, death of the patient was thought to be imminent. Following recovery, he still complained of attacks of piercing pain in the arms and legs and of roaring noises in his ears, but these gradually cleared up. Considerable criticism of manufacturers using carbon tetrachloride in their products, without sufficient warning of its dangers, was voiced by the author.

An unusual case of carbon tetrachloride poisoning in which the blood from the heart and large pulmonary arteries showed an extremely high percentage of fat (up to 60 per cent) was described in detail by F. B. MacMahon and S. Weiss (Am J. Path. 5:623 (Nov) 1929). The injury to the liver, which was quite severe and which showed fatty degeneration, was regarded as the source of the fat in the vascular system. The same authors have observed that patients suffering from alcoholism are more sensitive to carbon tetrachloride than others.

**CARDIOSPASM.**—In 1821 the first case of dilatation of the esophagus without obstruction was described by Purton, according to A. F. Hurst and G. W. Rake (Quart. J. Med. 23:491 (July) 1930). These authors point out that the first esophagosopic examination done in this condition occurred in 1895 and the first x-ray examination was made in 1897.

**ETIOLOGY.**—Various theories of etiology have been suggested, including

chest trauma, catarrh of the esophagus, compression of the esophagus in cardiac hypertrophy and weakness of the esophageal musculature. The first suggestion of a nervous pathogenesis was made in 1888, by Kronecker and Meltzer. Meltzer believed that a spasmodic contraction of the cardiac sphincter was responsible for the characteristic dilatation and hypertrophy, a theory which still receives support in American literature. Einhorn suggested a lack in the reflex relaxation or opening of the cardia during the act of swallowing. This view is the one held by the present authors, who introduced the term *achalasia* (absence of relaxation) in 1915. Mechanical effects of structures lying outside, or abnormal anatomical relations have also been suggested as causes of the condition. Hill and Jackson believe that the fault lies in the muscle-bundles of the diaphragm which encircle the esophagus at the hiatus, Hill suggesting an absence of normal relaxation of the diaphragm on swallowing, and Jackson believing that a phrenospasm is responsible.

The authors state that a study of swallowing function by x-rays has convinced them that "the last inch or more of the esophagus has such a totally different function from that of the remainder that it deserves to be regarded as a functional sphincter, whether an anatomical sphincter—a true condensation of circular muscle separating the esophagus from the stomach—exists or not." This sphincter offers a definite resistance to the passage of food, whereas the rest of the esophagus offers no resistance at all, according to the writers. The nerve supply of the esophagus is still under controversy, but it is generally admitted that both sympathetic and vagal fibers are involved.

Hurst and Rake (*loc cit*) state that 4 abnormal conditions may affect the cardiac sphincter. Overaction of the vagus would produce a patulous condition of the sphincter with increased tone above, while destruction of the vagus would produce inhibition of the sphincter which would then remain closed in front of a bolus of food. On the other hand, sympathetic stimulation would produce true spasm of the sphincter, while destruction would allow unopposed vagal action, according to these writers. The second and fourth results must be caused by definite organic lesions, the first and third, however, may be produced reflexly from lesions elsewhere. Lesions of the second and third types, *vis*, vagal destruction, or sympathetic stimulation, would produce obstruction at the cardia. The writers doubt whether true cardiospasm ever occurs as a purely functional disorder, although it may result as a reflex from nearby lesions. Hypertrophy of the esophageal musculature results from the peristaltic activity attempting to overcome the obstruction. Extreme dilatation may result.

Hurst supports his views of achalasia by stating the experience of passing a mercury bougie into the stomach. The tube passes the sphincter very rapidly and can be withdrawn without any "gripping" on the part of the sphincter which, he states, would be impossible in case of true spasm. Hurst does not deny the occurrence of cardiospasm, but believes that such a condition is always reflex from some nearby lesion, and that the majority of cases so classified are in reality due to achalasia.

As to the immediate cause of the condition, the writers state "the majority of cases are caused by progressive

organic disease involving Auerbach's plexus" Rake has described his study of such cases showing subacute inflammatory lesions involving the plexus. In the final stages the ganglion cells are replaced by scar tissue, according to this observer. Such lesions have been found in every one of 11 cases studied up to the time of this publication.

Extreme degrees of dilatation are often present in achalasia, comparable to that of the colon in Hirschsprung's disease, or in idiopathic megaloureter, according to these authors. Hypertrophy of the esophageal muscle first occurs, later dilatation follows, due, these writers believe, to loss of tone resulting from disease of Auerbach's plexus. The dilatation usually extends to the level of the diaphragm, but occasionally reaches below. Hurst believes that this latter finding is strong evidence against the views of Hill and Jackson on etiology. Esophagitis is practically always present in chronic cases, resulting, the writers suggest, from the irritation of retained food. Ulcers, leukoplakia and wart-like nodules have been reported. Hypertrophy of the salivary glands is a common finding, according to the authors.

**DIAGNOSIS.**—Symptoms of achalasia usually appear suddenly, beginning with a feeling of food sticking beneath the lower end of the sternum. Regurgitation of bland undigested food frequently follows, with relief of the discomfort. At first, attacks are intermittent, but later the symptoms become constant. Similar symptoms are produced by cancer of the esophagus, or of the fundus of the stomach, but differ in that they are more insidious in onset and progress steadily until obstruction occurs. In achalasia, however, the obstruction is no more complete in 10

years than at the onset, the authors point out. X-ray is usually of more value than esophagoscopy, according to Hurst and Rake, although the esophagoscope may be needed to rule out local lesions in some cases.

**TREATMENT.**—The treatment suggested in this paper consists of **dilatation, treatment of the esophagus, and surgery.** The former is accomplished by means of **Hurst's mercury bougies.** It is recommended that the first passage be done under the fluoroscope. Later, the patient is taught to dilate himself prior to each meal. After a few weeks, the treatment can be gradually discontinued, except when some symptoms recur. Another method suggested is the use of the **Plummer hydrostatic pressure bag.** *Esophagitis* is best treated, according to the authors, by a **smooth diet, and lavage** by regurgitation or tube.

Surgical intervention is occasionally necessary and may consist of **retrograde digital dilatation**, or a type of **Rammstedt's operation** as in pyloric stenosis, both of which have been reported as successful in several cases.

In the American literature, H. W. Soper and L. D. Cassidy (Tr. Am. Gastroenterol. A. (1928) 31: 86, 1929) have reported studies on 60 cases of cardiospasm. A review of the literature revealed many suggestions as to etiology, most of the authors agreeing that disturbances of the nervous mechanism of the cardia are responsible for the development of the spasm. In the present series 29 patients showed associated pathology as follows:

Hyperthyroidism .. . . .	3
Gall-stones .. . . .	4
Carcinoma of stomach . . . . .	4
Ulcer, cardiac end of stomach . .	2
Spinal arthritis . . . . .	3



Duodenal ulcer	3
Pleural contractures involving the diaphragm	4
Ovarian cyst	1
Hypertrophic cirrhosis	1
Bronchial asthma	1
Neurosyphilis	2
Pyloric ulcer	1

## CARDIOVASCULAR SYSTEM.—ANGINA PECTORIS.—

**Etiology.**—In a study of the etiological correspondence between anginal pain and cardiac infarction, C F. Coombs (Quart J Med. 23 233 (Apr) 1930) reports the finding of cardiac infarction but once in 88 cases of cardioaortic syphilis—though pain of the type that characterizes ischemia cordis was presented by nearly half the cases. In only 1 case of active rheumatic carditis was there a typical ischemic syndrome; and of more than 100 cases of ulcerative endocarditis, only 1 had symptoms suggestive of coronary embolism. Substernal pain of the cardiac type is not infrequently excited by severe anemia (being observed in 8 of 36 cases of pernicious anemia). In the absence of coronary lesions at postmortem examination in these cases, the anemia itself is presumably responsible for the symptoms. The high incidence of the anginal syndrome in the syphilitic, senile and hypertensive groups is the result of damage to the structures concerned in the supply of oxygenated blood to the myocardium, *viz.*, the first part of the aorta, the aortic semilunar valves, and the coronary arteries. The etiological mechanism is explained, as follows: (1) Lack of elasticity of the aorta diminishes its power to recoil in diastole and, thereby, force blood into the coronary arteries; (2) aortic insufficiency lowers the diastolic pressure in the first part of the aorta and lessens the

force with which blood is propelled into the coronary system, (3) changes in the coronary arteries themselves directly diminish the blood supply of the myocardium.

**Syphilis**—According to A S Warthin (Am Heart J 6 163 (Dec) 1930), syphilis of the coronary arteries involves most frequently the smallest intermuscular branches, and only rarely are the main divisions the seat of active syphilitic lesions. In about 50 per cent. of cases the *Spirocheta pallida* was demonstrated in the characteristic perivascular infiltrations of lymphocytes and plasma cells around small vessels (with obliteration of the arterioles and resultant fibrosis). Secondly and not primarily, syphilis is an important factor in the production of coronary disease and its concomitant angina pectoris. Coronary sclerosis, coronary occlusion and thrombosis, myocardial infarction and angina pectoris were found more frequently in the latent syphilitic than in the nonsyphilitic, and sudden cardiac death was almost 5 times as frequent in the syphilitic as in the nonsyphilitic autopsies. In the majority of cases, sudden death was due to cardiac insufficiency and dilatation, resulting from a diffuse interstitial myocarditis of slight degree, leading eventually to fibrosis.

**Nervous and Mental Influences**—S R Roberts (Am. Heart J 7 21 (Oct) 1931) states that nervous and mental influences are probably more closely connected with angina pectoris than with any other disease of the circulation, with the possible exception of essential hypertension. He agrees with other authorities that angina occurs much more frequently than in the not remote past. "In 1931, in Atlanta, among the better class of whites, particularly over 50, it is common. Among

the negroes subject to every other form of cardiac and coronary disease except the influence of nervous and mental strain, it is practically unknown" In 20 years' experience among sick negroes in both in- and out- patient sections Roberts never saw a case of angina pectoris in a negro Deaths from angina apparently are nearly twice as frequent in the Northern and Eastern States as in the Southern and Mid-western States, and the rarity of angina in the slow-going tropics is well-known A probable explanation for the smaller incidence of angina among negroes is the fact that they are seemingly less highly organized nervously "The white man, particularly those living lives of stress in urban conditions of competition, work and strain, makes his little plans and lays up cares and riches and takes much thought of the morrow; the negro knows his weekly wage is his fortune, takes each day as it is, takes little or no thought for the morrow, plays, and lives in a state of play, hurries none and worries little" Neither does the Chinaman have angina—with "the placid inner life of the Oriental, reinforced by thousands of years of custom and inner peace, and accented by his nature, 'this tranquil quietist.'" (Roberts refers to the article, "Spasmogenic Aptitude," by W. R. Houston *M. Clin. North America* 12. 1285 (Mar.) 1929) The relative rarity of angina in women is also suggestive of the weight of nervous and mental influences in precipitating the condition.

J B Herrick (*Am Heart J* 6 589 (June) 1931) believes that the close association of the symptoms of angina pectoris and coronary thrombosis is something more than accidental, and that each is clearly associated with a suddenly developed anatomical change

in the coronary artery and not in the aorta In subscribing to the coronary theory, he does not deny that a diseased aorta may cause a pain which at times resembles that of coronary angina, but that often lacks the earmarks of the typical form He does not agree with Wenckebach that previous anginal pain generally ceases after an extensive infarction More coronary lesions would be found postmortem if the vessels, including the smaller branches, were examined more closely, however, the absence of a demonstrable coronary lesion does not exclude arterial spasm

In a paper entitled, "Angina Pectoris. Is it Always Due to Coronary Artery Disease?" T McCrae (*Am J M Sc* 179 16 (Jan) 1930) stresses the point that angina pectoris is a clinical syndrome with fairly marked features but without any definite single causal pathologic change, and, therefore, should be clearly distinguished from acute coronary artery occlusion, which has a definite pathologic basis Attacks of angina pectoris and coronary occlusion do occur at times in the same patient However, if every attack of angina pectoris is due to coronary artery disease, what happens to the patients who have severe attacks for many years? He cites as an example a patient who suffered many attacks over a period of 14 years and then died without any evidence of serious cardiac change. In a case of this type coronary spasm might have played a rôle. The group of cases suffering anginal attacks associated with esophageal or gastric symptoms are well-known An example is a patient, aged 67 years, whose attacks occurred for a period of 4 years, each beginning with a feeling of distention and a desire to belch, soon followed by pain—relief being obtained by passing a stomach tube

at the first sign of any distress. In another case, an anginal attack was occasioned by a biliary drainage. Such attacks might be due to reflex spasm of the coronary arteries, but, in the mind of the author, it does not seem likely that a patient, aged 67 years, has coronary arteries which are capable of much spasm.

At times, angina pectoris is apparently secondary to disease elsewhere in the body. For example, a man, aged 47 years, had suffered for 2 years attacks of thoracic pain, growing more frequent and more severe, death being feared in each attack. Examination revealed no evidence of any disease of the circulation, but there was found a severe prostatitis with inflammation of the verumontanum with marked tenderness. Treatment of the latter condition was followed by rapid general improvement—with gradual disappearance of the attacks of thoracic pain and subsequent freedom from symptoms for the past 12 years. This case strongly suggests that a purely nervous mechanism is responsible for some anginal attacks. The author concludes that there are probably several factors in the aorta, the coronary arteries, the myocardium, and the nervous system which may be operative in causing an attack of angina pectoris, and he doubts that disease of any one structure can explain all cases.

**Pathogenesis.**—In recent years the coronary hypothesis as to the pathogenesis of angina pectoris has been seemingly definitely strengthened.

**Experimental Studies of Pain of Cardioaortic Origin.**—In an ingenious set of experiments D. C. Sutton and H. C. Lueth (*Arch Int Med* 45:827 (June) 1930) studied the physiologic effects of temporary occlusion of the coronary vessels in the unanesthetized

and anesthetized dog, the production of pain in the heart and blood-vessels, and the results of distention of the aorta, the aortic ring, and the peripheral vessels. Under ether anesthesia, with artificial respiration, a small incision was made in the parietal pericardium, through which a ligature was passed around the ramus descendens anterior sinister branch of the left coronary artery. Without being tied, the ligature was passed through a flanged tube, which led the ends to the surface. The tube was sutured in place and the incision was closed. After the animal had completely recovered from the anesthesia, observations were made of the effects of temporary coronary occlusion, produced by steadying the glass tube and drawing on the ligature.

These workers found that (1) the moment the artery, vein, or both, were compressed, pain, shown by the restlessness of the animal, occurred, but ceased immediately the compression was released. (2) Seemingly, the severity of pain varied not only with the degree of obstruction, but also with the size of the vessel occluded (the larger the artery, the greater the pain). (3) Traumatism of the myocardium and visceral pericardium did not cause any evidence of pain. Even cutting entirely through the myocardium and visceral pericardium by pulling on the ligature failed to produce pain. Stretching of the parietal pericardium by traction on the glass tube and displacement of the heart did not produce pain. (4) Pain ceased immediately when the artery was torn in two with the ligature. (5) Pain was not occasioned by compression of a vessel which had been carefully dissected out and painted with 80 per cent. alcohol to destroy the closely associated nerve fibers. (6) Section of the

vagi did not alter the pain resulting from occlusion of the artery (7) Salivation (accepted as evidence of nausea in the dog) was observed repeatedly during the compression (8) Removal of the annulus of Vieussens completely abolished all pain resulting from compression of the vessels (9) Electrocardiographic studies showed various types of arrhythmia to accompany temporary coronary occlusion There also was observed a marked increase in the amplitude of both the R and T waves Inversion of the T wave occurred only once, but in all cases it arose before the end of the down stroke of the R wave. (10) In the anesthetized dog a rapid fall in blood-pressure, amounting to from 30 to 50 mm of mercury, immediately followed partial obstruction of the vessels

In view of points (4) and (5) it appeared that the pain occasioned by experimental occlusion of the coronary artery is transmitted by nerve fibers present in the adventitia of the coronary artery or in the immediate surrounding tissues These points also afforded evidence against the idea that the pain in occlusion may be produced by the sudden distention of the artery proximal to the point of occlusion.

To exclude the possibility that pain produced was due to compression of the nerves and not due to ischemia below the occlusion, one or the other of the coronary arteries was blocked at its origin by passing a wire with a small knob on its end down the left coronary artery and through the aorta. Closure of a coronary orifice in the aorta immediately caused pain Sudden death from ventricular fibrillation occurred at times Pain ceased as soon as the obstruction was removed. Trauma of the aorta and valve cusps did not produce

pain This procedure indicated that pain of experimental occlusion is not the result of pressure on the nerves included in the ligature, nor of sudden distention of the coronary arterial wall proximal to the point of occlusion

To test the aortic hypothesis of Vaquez, Allbutt, Wenckebach and others, *viz*, that the pain of angina pectoris is produced by dilatation of either the first portion of the aorta or the aortic ring, a set of experiments was performed in which the aorta, aortic ring, and other vessels were dilated with a specially constructed dilator Under local anesthesia, the dilator was passed down the left carotid artery into the aorta. It was found that pain was not produced by any of the following maneuvers. (1) Stretching the ascending aorta, even to the point of cutting the intima; (2) dilating the aortic ring; (3) dilatation of the carotid artery, (4) perforation of the carotid artery, the aorta, the aortic ring, or an aortic valve cusp; (5) dilatation of the left ventricle. Dyspnea followed dilatation of the ascending aorta, aortic ring and left ventricle, varying with the amount of dilatation Pain followed perforation of the aorta when a sufficient quantity of blood had collected in the mediastinum to produce marked stretching of the limiting tissues. In no instance did dilatation of the ascending aorta produce a fall in blood-pressure that would indicate the stimulation of a depressor nerve

These experiments throw much light on the mechanism of the production of the pain of angina pectoris and on cardioaortic sensation, about which there is so much uncertainty. If these observations can be applied to man, the coronary hypothesis that anginal pain arises as the result of ischemia of a re-

stricted part of the myocardium must be accepted without question.

***Electrocardiographic Changes.***—

F C Wood and C C. Wolferth (Arch Int Med 47 339 (Mar) 1931) state that the trend of current opinion is toward the belief that the majority of cases of Heberden's angina can be explained on a coronary basis; but that the main difficulty confronting this explanation has been the lack of direct evidence that the heart is primarily involved during the paroxysm. In the minds of these workers the changes in the ventricular complexes of the electrocardiogram recorded by various investigators in patients during anginal attacks are not sufficient evidence to justify the conclusion that all angina is coronary in origin.

Wondering as to whether the electrocardiographic changes are indicative of a specific change in the heart, such as a temporary myocardial ischemia, or whether they are merely due to the exercise which provoked the attack or the changes in blood-pressure or pulse rate which accompanied it, attacks of angina pectoris were studied in 30 patients. In 6 cases the attacks were spontaneous, and in 24 cases the pain was induced by varying amounts of prescribed exertion.

In an attempt to rule out exercise and alterations in blood-pressure or pulse rate as factors in the production of the electrocardiographic changes, the effect of various amounts of exercise on the electrocardiogram was observed in 100 normal subjects, in 50 patients with cardiovascular disease other than angina, and in 12 patients with histories of anginal attacks in whom the prescribed exertion was not productive of a paroxysm, and also the effect of paroxysmal pain known to be due to an extracardiac lesion was studied in 4

cases (ureteral colic, distended bladder, duodenal ulcer, and diaphragmatic hernia). In none of the control subjects did exercise cause a deepening of an inverted T wave, a definite inversion of a flat T-wave, or a deviation of the S-T interval from the iso-electric line.

With these observations as a background for comparison, it was found that 15 (50 per cent) of the angina pectoris patients showed definite temporary alteration in the ventricular complexes during the pain, unlike any seen in the control series, and that the remaining 15 showed no "specific" electrocardiographic changes during the attacks. In most of the cases the alteration in the ventricular complexes were most pronounced when the paroxysm was at its height, and disappeared within a minute or two after the pain subsided.

Seemingly, the severity of the pain was not the main factor that determined the presence or absence of specific electrocardiographic changes during the attack. The authors feel that it is reasonable to suspect (though it cannot be considered proved) that some intrinsic change takes place in the heart itself during the paroxysm which causes the changes in the electrocardiogram.

To decide whether or not the phenomena of an anginal attack can be explained on the basis of a temporary interference with the blood supply of a part of the heart muscle, these workers studied the effects of temporary coronary artery occlusion with clamps or ligatures in animals. It was found that such occlusion may produce temporary and rapidly reversible electrocardiographic changes analogous to those observed in angina pectoris; and that these changes may appear and disappear within 2 minutes, a period of time com-

parable to that involved in an anginal attack. Factors of seeming importance in the production of the striking electrocardiographic changes were as follows: (1) The particular vessel occluded, in general, more striking changes following the clamping of vessels on the posterior surface of the heart, *ie*, the circumflex branch of the left and the posterior descending artery; (2) the size of the area of myocardium with interrupted blood supply, more marked changes following simultaneous obstruction of both main branches of the left coronary (the anterior descending and the circumflex) than obstruction of either one separately; (3) simultaneous obstruction of accompanying veins; (4) the state of the heart before the occlusion—occlusion in a healthy fresh heart not producing electrocardiographic changes so readily as in a damaged organ; (5) the duration of the occlusion—the longer the occlusion, the more pronounced the changes in the ventricular complexes.

The results of their study favor the coronary hypothesis as to the pathogenesis of angina pectoris; however, the authors admit that the evidence presented does not rule out the possibility that paroxysms of precordial or substernal pain may be the result of other mechanisms.

J. Parkinson and D. E. Bedford (*Lancet* 1:15 (Jan. 3) 1931) found definite changes in the ventricular complexes of electrocardiograms of 5 patients during attacks of angina pectoris. These changes were transitory, consisting of a depression of R-T and a diminution in the amplitude or inversion of the T-waves in one or more leads (closely resembling, though not so pronounced as those occurring in the early stages of cardiac infarction).

**Complications.**—*Diabetes and Angina Pectoris*—H. F. Root and A. Graybiel (*J. A. M. A.* 96:925 (Mar 21) 1931) report the incidence of 210 cases of angina pectoris in a group of 7000 cases of diabetes mellitus in Joslin's clinic. Of these patients, 122 were males and 88 were females, in contrast to the usually much greater proportion of males (which in general is about 3 to 1). The average age at onset of the angina was found to be a little greater in the diabetic than in nondiabetic individuals, possibly owing to the fact that the commonest age for the onset of diabetes is generally 51 years, and that, on the average, angina develops from 9 to 10 years later. The average blood sugar for the entire group was 0.17 per cent. Hypertension, with a systolic pressure above 150, occurred in 110 patients. Some degree of coronary sclerosis was found in every case in which diabetes had been present 5 or more years; and actual thrombosis with infarction of the heart was present in 25 per cent of the 100 autopsies. The authors found that sudden reductions in the blood sugar, by change in diet or by insulin, had a tendency to increase the frequency and severity of the anginal attacks. In the 136 fatal cases the average duration of life from the first attack of angina to death was only 2 years (which is definitely shorter than in the general nondiabetic series of White and Bland).

**Diagnosis.**—S. R. Roberts (*loc. cit.*) states "it is probably as important to realize what is not angina as it is to recognize angina." The various types of thoracic pain may be grouped, as follows, according to Roberts:

1. Angina pectoris is a paroxysmal thoracic complaint, not necessarily associated with demonstrable heart or aortic



disease, ranging in radiation from the epigastrium to the tips of the fingers and even more distant parts, varying in degree from a simple substernal weight or sensation, through an ache to a tearing pain or a collapsing agony, and associated in the mind with a sense of danger or dying. It occurs usually in the sensitive, nervous type, as the Jew, or in the tense, efficient American, rather than in the dull, happy negro or the calm, accepting Chinaman. There is no characteristic electrocardiogram. [See abstract of Wood and Wolferth's article on *Electrocardiographic Changes*—Ed.]

2 The pain of coronary thrombosis, of a location and radiation similar to angina, but of longer duration and associated with fever, leukocytosis and often a pericardial friction rub. Much argument hinges here, but coronary thrombosis is probably a different disease from angina, and the latter is but one of the symptoms of the former. An infected vegetation in the pulmonary artery gives substernal pain. Coronary thrombosis has a characteristic electrocardiogram.

3 The pain of acute aortitis, syphilitic or rheumatic in nature as a rule, usually substernal in location and anginal in kind. This pain is probably to be regarded as dependent on infection and a cellular pathology in the aorta, and as one of the symptoms of an acute aortitis.

4 The precordial pain of organic heart disease, valvular disease, and heart failure. It may occur in the big, brave heart of a hypertension before or after actual congestive failure. The pain may be referred rather gently to the left shoulder and arm, or appear as a dull ache in the region of the left scapula. It is but a symptom of the underlying disease and failure of the heart.

5 Precordial pains usually transient, but recurring for weeks or months or even years in neurotic patients, more frequently in women. The location of the pain is rarely substernal, more often apical or precordial.

6 Cases of neurocirculatory asthenia, the effort syndrome of the English, the "soldier's heart" of the Civil War. Here the evident relation to stress and fear (whether in war or peace), the precordial pain, tachycardia, fatigue and even mild cyanosis, make a distinctive picture that needs time, rest and encouragement for recovery.

7 Aches and pains involving the tissues of the left chest wall. Here belong hyperesthesia of the skin, panniculitis of the adipose tissue, fibrositis of the connective tissue, myalgia of the intercostal muscles, intercostal neuralgia, and referred pain from other areas and trauma. "Would you be uneasy if the same pain were on the right side?" is a good question.

8 The pains of the grosser lesions—pericarditis, pleurisy, empyema, aneurism, mediastinal growths, lung tumors, and referred pains from disease of the cord and vertebra.

9 Many exceedingly rare conditions occur in the chest. A phlebitis of the thoracoepigastric vein is a case in point. Pain substernal or precordial in location is of particular importance for diagnosis.

*Adrenalin Test*—S. A. Levine, A. C. Ernstene and B. M. Jacobson (*Arch Int Med* 45 191 (Feb) 1930) suggest that the production of anginal attacks subsequent to an injection of 1 c.c. (16 minims) of adrenalin subcutaneously may serve as a diagnostic test for angina pectoris. Typical pain resulted from such injection in all but 1 of 11 patients with angina pectoris, and in

none of 20 control patients. A somewhat greater increase in blood-pressure and pulse rate occurred in the anginal group than in the others. In view of the fact that adrenalin produces typical pain with great regularity in patients with angina pectoris, the therapeutic use of the drug in such patients should be carried out with great caution. This particular test should not be made in cases of angina pectoris when the diagnosis is certain, but should be reserved for doubtful cases (in which there are other possible explanations for the symptoms, such as disease of the gall-bladder, stomach or the duodenum).

The serious results which might attend this diagnostic procedure are strikingly shown in the case reported by J. E. Cottrell and F. C. Wood (*Am. J. M. Sc.* 181:36 (Jan.) 1931). In a patient with a history of attacks of substernal pain, radiating down the left arm, subcutaneous injection of 1 cc (16 minims) of 1:1000 adrenalin resulted in a violent attack of substernal pain persisting for over 8 hours, with collapse, unconsciousness, bradycardia, cessation of respiration and a fall in blood-pressure from 170/115 to 80/60. This narrowly averted disaster should tend to curb any overzealousness in the use of this diagnostic procedure.—Ed.

**Prognosis.**—In a series of 500 patients with angina pectoris studied by P. D. White and E. F. Bland (*Am. Heart J.* 7:1 (Oct.) 1931), 213 have died, with an average duration of life of 4.4 years after the onset of the disease. The average duration of life to date for the entire series of 500 cases is 4.9 years. Of the patients who died, death could be attributed to failure of the heart in 82 per cent., sudden death being quite a frequent occurrence. The average age at death for the group was 62.2

years. Of 393 patients who had electrocardiograms, 74 (19 per cent) showed normal hearts on physical examination (in size, sounds, rate and rhythm), normal blood-pressure and normal electrocardiograms, which combination of findings has proved an unusually favorable prognostic sign.

Coronary thrombosis, although frequently encountered (about 25 per cent), did not affect appreciably the duration of life, provided the patient survived the acute attack. Hypertension was present in 182 (36 per cent) of the 500 patients, but apparently was of no serious import. The electrocardiogram was of little help in predicting the outcome, however, a "coronary" type of T wave in Leads I or II occurred more often in the patients who died early.

Evidence of arteriosclerosis, by physical or x-ray examinations, was a frequent finding, occurring in considerably more than half of the patients. Syphilis was present with certainty in only 22 patients (5.5 per cent). A history of rheumatic fever was presented by 37 patients, with apparently no effect on the prognosis.

Of the total series, auricular fibrillation was present in 19 cases (which fact is of interest, in that it is generally recognized that angina pectoris and auricular fibrillation are rarely present at the same time). In 11 patients arrhythmia of this type occurred in paroxysmal form, in 4 it was a terminal event; and in the remaining 4, both it and angina were constantly present. Two patients had angina pectoris at the time of their paroxysms of auricular fibrillation, an unusual combination—easily confused with acute coronary thrombosis. One patient with arteriosclerosis and hypertension has had complete auriculo-

ventricular heart-block for 35 years, with slight congestive failure at intervals, and continues to have angina pectoris on exertion, but remains in fair condition

The presence of syphilis, angina decubitus, poor heart sounds, definite cardiac enlargement, congestive failure, or marked arteriosclerosis appear to be unfavorable, and the more of these factors present in a given case, the worse the prognosis. Care of the health is a vital factor in the prognosis. The establishment of a regimen of proper rest, diet, and exercise (with avoidance of strains of all kinds) tends to prolong life, sometimes for years.

**Treatment.**—S R Roberts (*loc cit*) urges that the real curative and preventive treatment of angina pectoris is to treat the anginous state. Though the heart be the location of the attack, the nervous and mental processes may be the source of the anginous state, the attack may be viewed as a "flash of lightning in a clouded sky." Merely to treat the attack is to view the patient bodily, not as a personality, and does not in the least lessen the drive of life that, perhaps more than any other factor, causes the angina. Roberts wonders whether nerve injections and resections, except for the relief of agonal angina after every other measure has been tried, are not the wrong course for anginal therapeutics.

**Paravertebral Alcohol Injection.**—In a report of 18 cases of angina pectoris treated by paravertebral alcohol injection and 3 treated by surgical operation, J C. White (Am J Surg 9:98 (July) 1930) gives an excellent discussion of the merits and shortcomings of these procedures. A thorough knowledge of the anatomy of the cardiac nerves is most essential before attempting either

operation. The fundamental anatomical facts about the sensory-motor nerve supply of the heart are as follows:

"Sympathetic afferent and efferent impulses enter and leave the spinal cord over the white communicant rami of the upper fifth to sixth dorsal segments. Below this level, impulses go to the splanchnic system, above, in the neck, there are no white rami, and, therefore, no connections between the sympathetic trunk and the central nervous system. The white rami leave the dorsal nerves just as the latter emerge from their intervertebral foramina. They then run a short distance below the pleura to the chain of sympathetic ganglia which lie on the anterolateral surface of the vertebræ. It is in this region that the cardiac impulses can be most effectively interrupted by alcohol block or surgical section, because the entire nerve supply to the heart lies concentrated here in the upper 5 to 6 pairs of white rami and the corresponding chain of dorsal sympathetic ganglia.

"From this point on, the pathways become infinitely diverse and complex. One part ascends to the stellate ganglion and the cervical trunk, to be relayed back to the heart over the superior, middle and inferior cardiac nerves. Between these fibers and the vagus there are numerous anastomoses. A second and very important group of postganglionic fibers leaves the upper dorsal sympathetic trunk, chiefly from the second, third and fourth ganglia, and run directly across the posterior mediastinum to the heart."

Alcohol block should be considered particularly in the treatment of patients suffering attacks so severe that life is almost unbearable. The presence of any active sepsis should contraindicate the procedure, as the sterile areas of alcohol necrosis might become infected through the blood stream and set up a serious mediastinitis. Advanced cardiac decompensation would render injection dangerous, but under these circumstances angina is usually absent. Mild

decompensation and previous attacks of coronary thrombosis are not contraindications to injection. Any tendency for patients to overdo in the absence of the danger signal of pain, as mentioned by Mackenzie, has not been found. Shortness of breath, peculiar sensations in the region of the heart—without pain—or milder attacks on the right side, give adequate warning.

The *method of injection* consists in first infiltrating 2 c c (32 minims) of 2 per cent procaine around the trunks of the upper thoracic nerves as they emerge from the intervertebral foramina and give off their sympathetic rami. Sabat's second technic for inducing paravertebral anesthesia is used. The needles are not moved, and as soon as intercostal anesthesia develops, proving that they are accurately placed, 5 c c (1½ drams) of 95 per cent alcohol is injected into each.

The procedure is difficult technically because of the depth of the rami and the small area sclerosed by the alcohol. However, its results are distinctly better than in cervical sympathectomy. Of 18 cases treated by injection, 47.4 per cent. have been over 90 per cent improved; 26.3 per cent have been improved over 50 per cent, 10.5 per cent were only slightly relieved, and 15.8 per cent were failures. Five patients have been able to return to work. Three patients injected between 2 and 3 years ago still report complete relief on the injected side. In only 2 cases has there been a tendency to relapse. A patient with aneurism of the ascending arch of the aorta was totally relieved of pain referred over the entire cervical and upper dorsal region on the right side by block of the first and second dorsal rami.

G. I. Swetlow (Am J. Surg 9:88 (July) 1930) reports prompt and satis-

factory relief in all but 4 of 22 cardiac patients, suffering from attacks of severe precordial pain, treated by paravertebral alcohol injections of the dorsal root ganglia. Freedom from pain following a single injection usually lasted several months.

The worst *after-effects* observed by White (*loc cit*) to date have been 1 fairly severe and 2 milder attacks of *pleural irritation* from the alcohol, which disappeared within 24 hours. A troublesome factor has been a constant *skin irritation*, beginning as an anesthesia which after about a week is replaced by hyperesthesia, lasting from 2 to 6 weeks. This feature may be extremely annoying, particularly in the unsuccessful cases. The majority of the successful cases have shown other signs of sympathetic nerve block, such as Horner's syndrome, vasodilatation and cessation of perspiration in the arm. The chief complications after injection noted by Swetlow (*loc cit*) were 1 case of *pneumothorax*, and 5 cases of *intercostal neuritis* lasting from 1 to 40 days.

*X-ray Treatment*.—In a review of the literature, M. L. Sussman (Am J Roentgenol 24:163 (Aug) 1930) found the earliest reference to paravertebral irradiation in the treatment of angina pectoris to be the work of Groedel in 1923. In a series of 16 patients with severe angina pectoris, on whom treatment with paravertebral short wave radiation was started 5 months previously, Sussman reports almost complete relief in 6, and moderate improvement in 5 cases. Four patients had not returned for observation, and 1 died. He feels that the results warrant the continuation of the method of treatment.

*Surgical Treatment*.—All of 3 cases treated by White (*loc. cit.*) by **resection**

of the upper dorsal sympathetic ganglia were completely relieved of the left-sided angina. However, it is only the rare anginal patient (the milder types) who should be allowed to undergo this more radical surgical procedure because of the greater risk involved. The author feels that with improvement in the technic of alcohol injection, resection will no longer be necessary.

#### CARDIAC ARRHYTHMIAS.\*—

##### *Sinus Arrhythmia in Old People.*—

J M Faulkner (Am J M Sc 180 42 (July) 1930) calls attention to the fact that sinus arrhythmia in patients over 50 years of age is more frequently associated with evidence of organic heart disease than is normal rhythm. Faulkner's findings suggest the probability of 2 distinct types of sinus arrhythmia, with a different mode of origin, *i e*, (1) a youthful type which is directly related to normal phasic variations in vagal tone corresponding to the phases of respiration, and (2) a type occurring in older people which seemingly has no relation to the respiratory rhythm. The latter type may represent a reflex response to abnormal efferent stimuli from a diseased heart or aorta (in accordance with the suggestion of A M Wedd (Am J M. Sc 162 49 (July) 1921)).

***Paroxysmal Ventricular Tachycardia.***—In an analysis of 63 cases of paroxysmal ventricular tachycardia found in the literature and of 2 of his own cases, M B Strauss (Am J M Sc 179 337 (Mar) 1930) found that 84 per cent of the patients were suffering from organic heart disease, and that 60 per cent of these had been treated with digitalis prior to the onset of the tachycardia. In a number of cases the stopping of digitalis therapy was fol-

lowed by a cessation of the tachycardia, while its subsequent use resulted in a return of the rapid rate, which fact suggests that in the presence of organic heart disease this arrhythmia may be a toxic manifestation of digitalis. Strauss states that suspicion of the presence of paroxysmal ventricular tachycardia should be aroused whenever a rapid, almost or completely regular, rate supervenes in a case of long-standing heart disease, particularly if large doses of digitalis have been administered, or in a case of coronary occlusion. Also the quality of the first heart sound may perceptibly vary in different cycles, and vagal stimulation and ocular pressure are never effective in terminating a paroxysm of ventricular tachycardia. Positive diagnosis, however, can be made only by the electrocardiograph.

***Prognosis.***—In the absence of gross cardiac disease this type of arrhythmia does not give a bad outlook. However, of 50 cases with organic heart disease, 40 died within 3 hours to 6 months after the onset of the tachycardia (an average of 24 days). Most of the latter patients had received no specific treatment. Of 16 cases receiving quinidine only 3 died.

***Treatment.***—Quinidine (usually used as the sulphate) is the only therapeutic measure which has proved successful in terminating ventricular tachycardia. Paroxysms were controlled in all 16 cases in which it was employed. Doses as high as 7.5 Gm. (2 drams) daily have been administered, while maintenance has been possible at times on as much as 0.2 Gm. (3 grains) per day. Dosage must be adjusted to the individual case, the administration being repeated every few hours until the paroxysm is controlled or alarming symptoms disappear.

\* See also Electrocardiography

**Paroxysmal Auricular Fibrillation.**

—In a study of 200 cases of paroxysmal auricular fibrillation by J Parkinson and M Campbell (Quart J Med 24 67 (Oct) 1930), the attacks were classified, as follows (1) Typical recurrent paroxysms (more than half of all the cases), (2) a few paroxysms preceding the onset of established fibrillation, (3) single or very occasional paroxysms, often of longer duration, as occur in the course of congestive heart failure, after coronary thrombosis, with infections (as pneumonia), or with no apparent cause

**Etiology**—Structural heart disease—due in about equal proportions to rheumatic fever, hypertension, or primary myocardial disease—was present in 70 per cent of the cases observed by Parkinson and Campbell (*loc cit*), in 15 per cent goiter was the causative factor, and in 15 per cent no underlying cardiac disease was apparent

W M Fowler and F M Smith (J Clin Investigation 10 178 (Apr 20) 1931) report 10 cases in which auricular fibrillation was the only evidence of cardiac disease. The oldest patient was 34 years of age. The arrhythmia of 1 case was attributed to stimulation of the external auditory canal, 1 to exertion; 4 to alcohol, 1 to carbon monoxide; 1 to ether anesthesia, and 2 were attendants in gasoline stations. In 7 the arrhythmia was paroxysmal, while in 3 it had persisted from 2 weeks to 2½ years. Sinus rhythm was restored in the 3 latter cases by quinidine. The patient with the arrhythmia of 2½ years' duration later came to autopsy, and the heart was regarded as normal.

**Prognosis**—The immediate attack seldom persists more than 2 days. When it lasts a week, permanent fibrillation becomes much more likely, and

after 2 weeks almost certain. If a long interval of freedom follows the first few attacks, the prognosis is good, according to Parkinson and Campbell (*loc cit*) since there might not be a recurrence for years, or not at all, particularly when there is no other evidence of heart disease. In the presence of rheumatic heart disease permanent fibrillation is more likely.

**Treatment**—An attack of auricular fibrillation which has been present for more than 2 or 3 hours can often be arrested with quinidine. Digitalis should not be prescribed, in the opinion of Parkinson and Campbell (*loc cit*), because of its slower action and because it may prolong the attack. However, if quinidine proves ineffective, digitalis should be used, especially if congestive failure supervenes; but it is rarely indicated unless an attack has persisted for a number of days. Between the attacks, when they recur often enough to require treatment, and when no remediable cause such as a hyperthyroidism can be found, quinidine should be administered. In the absence of contraindications, as much as 5 grains (0.3 Gm) 3 times daily should be given. If quinidine proves unsuccessful, and if general measures fail to relieve the attacks, most patients would be well advised to bear with them; however, if the attacks prove unbearable, digitalis should be given in moderate doses. Even if permanent fibrillation is induced by digitalis, some patients find themselves better so. **Surgical operation is indicated in goiter patients in whom paroxysmal auricular fibrillation is a troublesome complication.**

**Chronic Auricular Fibrillation.—**

**Etiology**—In a study of 253 cases of chronic auricular fibrillation by W. D. Stroud, L. B. LaPlace and J. A.



Reisinger (Tr A Am Physicians 46 52, 1931, Am J M Sc 183 48 (Jan) 1932), 122 cases (48 per cent) belonged to the rheumatic group, 88 (35 per cent) to the arteriosclerotic group, and 43 (17 per cent) to a miscellaneous group. One hundred and sixty-four (65 per cent) of the patients were males and 89 (35 per cent) were females. The average age of onset of fibrillation due to rheumatic cardiovascular damage was 39 years.

The average age of onset of auricular fibrillation in the arteriosclerotic ("non-rheumatic") group was about 59 years. Of the 88 patients in this group none began to fibrillate before the age of 40 years, and 72 per cent began after 53 years. Auricular fibrillation was found comparatively rarely associated with syphilitic cardiovascular disease.

*Prognosis* — Stroud, LaPlace and Reisinger (*loc cit*) believe that the presence of auricular fibrillation does not necessarily imply a worse prognosis than in the nonfibrillating heart with an equal amount of cardiovascular damage. The prognosis was found to be very poor when fibrillation set in before the age of 25 years. In a chart of 77 rheumatic patients, 51 (66 per cent.) suffered their etiologic infection before the age of 20 years. Thirty-seven (73 per cent.) of the latter number began to fibrillate between the ages of 20 and 40 years, and in this group the average duration of life was about 3 years thereafter; 7 (13 per cent) began to fibrillate before 20 years of age, and their subsequent duration of life was less than 1 year, and the remaining 7 (13 per cent), whose arrhythmia started after 40 years of age, fibrillated for an average of 5 years. Eighty-eight per cent. of the patients with manifestations of rheumatic heart disease before the

age of 25 years (of whom 86 per cent developed auricular fibrillation before the age of 40 years) died before the age of 53 years.

H Cookson (Quart J Med 23 309 (Apr) 1930) has found the expectation of life in auricular fibrillation greater in the arteriosclerotic (nonrheumatic) group than in the rheumatic group. In 23 rheumatic cases in which the age at onset of fibrillation was between 12 and 17 years, the average duration of life was 10 months, while in 16 cases in which the age at onset was between 28 and 38 years, the average duration of life was 6.5 years. Cerebral embolism occurred as frequently when the rhythm was normal as when fibrillation was present. In cases with partial heart-block, in whom the ventricular action was persistently slow without digitalis therapy, though quite irregular, the prognosis was better than in cases where digitalis was necessary to control the ventricular rate. Auricular fibrillation seemingly does not add to the gravity of a case in which complete heart-block already exists; and when the 2 conditions are combined, Adams-Stokes seizures occur very rarely. Bundle-branch block was found to render the prognosis worse. Premature ventricular contractions, occurring spontaneously without digitalis, did not affect the prognosis. The auricular oscillations of the electrocardiogram were generally smaller in the nonrheumatic than in the rheumatic group; but there was little evidence of any relation between the duration of fibrillation and the amplitude of these waves. In a series of 2000 cases of auricular fibrillation only 5 patients suffered concurrent angina pectoris (which fact is in accord with the view already widely held, *viz*, that that combination is very rare).

In coronary thrombosis the onset of fibrillation had a variable effect on the pain. In 4 of 10 cases of thrombosis the pain diminished or ceased with the advent of paroxysmal fibrillation, congestive failure appearing with the arrhythmia in 2 of the 4 cases, and in the remaining 6 cases pain persisted with the fibrillation, congestive failure occurring in 2 only.

Infective endocarditis and auricular fibrillation are very rarely combined, though, both, by themselves, are common sequelæ of rheumatic carditis.

Death was sudden in 9 of 86 cases who died in this series. Seven of the 9 patients had good functional capacity; there was no evidence of digitalis overdosage, in no case was the QRS complex of the electrocardiogram abnormal; no obvious cause of death was found in the 2 postmortem examinations performed. It is assumed that ventricular fibrillation may be the factor responsible for sudden death.

**Treatment**—In the treatment of patients with chronic auricular fibrillation digitalis usually proved most satisfactory. Only exceptionally was the restoration of normal sinus rhythm by quinidine of more apparent value to the patient. Stroud, LaPlace and Reisinger (*loc. cit.*) concluded that quinidine should only be used in those few cases of younger individuals with slight or no demonstrable cardiovascular abnormality other than the arrhythmia, or in thyrotoxic patients when a spontaneous return to normal sinus rhythm does not follow partial thyroidectomy. Sudden death following the use of quinidine occurred in 2 instances in their series. Quinidine may be said to possess definite value only in the cases where normal sinus rhythm is restored for a substantial length of time. It was noted

that the majority of patients with restored sinus rhythm were no less "heart conscious" than during the period of fibrillation under effective digitalis therapy.

**Bundle-Branch Block.**—*Etiology*—In a series of 41 cases of bundle-branch block studied by I. G. W. Hill (*Quart J Med* 24: 15 (Oct) 1930), most of the patients were suffering the degenerative type of heart disease with arteriosclerosis and hypertension. Congenital defects, rheumatic fever, and syphilis were rarely responsible for the condition.

An unusual cardiac mechanism, consisting of *functional bundle-branch block*, abnormally short P-R interval, and paroxysms of tachycardia (also paroxysmal auricular fibrillation and, perhaps, flutter), occurring mostly in otherwise healthy young people, is reported by L. Wolff, J. Parkinson and P. D. White (*Am. Heart J* 5: 685 (Aug.) 1930). The abnormality is seemingly largely due to vagal influences, since, spontaneously or following release of vagal tone by exercise or atropine, the ventricular complexes were found to revert to normal form and the P-R interval became of normal length. Auriculoventricular nodal rhythm was apparently not the cause of the short P-R interval. Infections, toxic states, and rapid heart rates appeared to have some etiological significance.

**Diagnosis**—In Hill's experience (*loc. cit.*) the diagnosis of bundle-block by means of physical signs alone is not feasible. J. T. King and D. McEachern (*Tr. A. Am. Physicians* 46: 39, 1931), however, consider that intraventricular block may be recognized in the majority of cases by physical signs. An analysis of 50 consecutive cases of bundle-branch block showed the following physical

signs. (1) Visible reduplication of the apex thrust in 42 (84 per cent), palpable reduplication in 40 (80 per cent), (2) the first sound split into 2 elements in 28 (56 per cent). There were 2 separate systolic murmurs in 6 (12 per cent), and a single first heart sound with a separate murmur in 8 (16 per cent). Presystolic gallop has a superficial resemblance to the signs of bundle block, however, clinical evidence and apex cardiograms show that presystolic gallop is entirely presystolic, and that the signs of bundle block are limited to systole, causing a division of the apex systolic plateau. A light straw fastened on the chest wall over the region of the apex impulse aided in demonstrating the phenomena occurring at the apex. On the basis of physical signs, a correct diagnosis was made prior to knowledge of the electrocardiogram in 34 of 40 attempts. In 3 cases with complete auriculoventricular block as well as intraventricular block, the clinical signs just described were quite clear, and in 5 of 7 cases of auricular fibrillation with bundle block the latter condition was recognized clinically. The latter 2 groups of cases show that the auricles are not concerned in the physical signs of bundle block.

*Prognosis*—The expectation of life in the cases observed by Hill (*loc cit*) was found to be not much over a year, however, some patients do live considerably longer. The poor prognosis is due to the fact that the bundle block occurs in severe degenerative myocardial disease. Therapeutic doses of digitalis and atropine did not produce any demonstrable changes in the ventricular complexes.

**DISEASES OF BLOOD-VESSLS.—Coarctation of Aorta.**—H. L. Blumgart, J. S. Lawrence and A. C.

Ernstene (Arch. Int. Med. 47:806 (May) 1931) studied the dynamics of the circulation in 2 cases of coarctation of the aorta (aged 47 years and 66 years respectively). The diagnosis was established in each instance by (1) evidence of extensive collateral arterial circulation observed on physical examination, and also made apparent by erosions of the ribs seen in the x-rays of the chest, (2) arterial hypertension in the arms as contrasted with the relatively low blood-pressure in the legs, and (3) diminution and retardation of the arterial pulses in the legs.

Physical examination and x-ray studies failed to disclose any difference in the degree of arteriosclerosis in the upper and lower portions of the body, even though arterial hypertension presumably had been present above the level of the coarctation in both patients for over 40 years. Furthermore, it is interesting to note that the arteriolar blood-pressure in the arms was found to be normal, which fact suggests that the arterial hypertension above the coarctation is due to the resistance offered by the constricted aorta and the collateral pathways. The velocity of blood flow in the larger arteries of the leg was reduced, and the arterial-arteriolar difference in blood-pressure was greatly diminished. However, according to the measurements of oxygen in the blood, the blood supply to the tissues of the lower extremities under resting conditions was within normal limits.

Attention is called to the fact that the first symptoms of a failing heart in patients with coarctation of the aorta may appear in the lower extremities (where the circulatory reserve previously has been impaired), in the form of intermittent claudication, nocturnal cramps and diminished temperature,

some time before the onset of dyspnea or other evidence of circulatory stasis

**Arteriosclerosis and Diabetes.**—E. P. Joslin (Ann Int Med 4 54 (July) 1930) has emphasized the remarkable effect of diabetes on the production of arteriosclerosis. According to his data, 37 per cent of the population as a whole die of arteriosclerosis, while in diabetes 48 per cent of deaths are due to this condition. The degree of arteriosclerosis increases with the duration of diabetes. Arteriosclerosis, however, develops in diabetic children; calcification of the arteries of the legs was present in 10 of his cases; and 1 child died with gangrene of a toe. Among patients with diabetes of less than 5 years' duration, 30 per cent die of arteriosclerosis; while of those who have had diabetes for 10 or more years, over 50 per cent die of arteriosclerosis. Of the total mortality from diabetes, 19.1 per cent is the result of arteriosclerosis of the heart; 13.2 per cent, of the legs, 7.2 per cent, of the brain, and 4.7 per cent, of the kidneys.

H. C. Shepherdson (Arch Int. Med. 45 674 (May) 1930) found x-ray evidence of arteriosclerosis in 18 (36 per cent) of 50 patients under 40 years of age who had had diabetes for at least 5 years. The average age of the entire group was 23.4 years, and the average duration of the disease 6.9 years. This author further points out that the average values of blood cholesterol in this group were lower than those obtained before the addition of insulin to diabetic therapy, and paralleling the reduction of lipemia the incidence of arteriosclerosis has been greatly reduced. This latter fact allows the assumption that altered fat metabolism is the morbid factor in the development of vascular disease in diabetes.

**Main Branches of Coronary Arteries in Rheumatic Fever.**—C. B. Perry (Quart J Med 23 241 (Apr) 1930) calls attention to the fact that the main branches of the coronary arteries are usually affected in rheumatic carditis. The lesion consists of a general panarteritis. The intima presents patchy areas of thickening with a loose connective tissue, more or less cellular; the changes in the media, also in patches, vary in intensity from a loss of nuclei in the muscle fibers to fairly dense cellular infiltration, with breaking up of the muscle cells and some vacuolation. The adventitia, in most cases, shows an increase in fibrous tissue and lymphocytic infiltration of varying intensity.

**Embolectomy.**—Occlusion of one of the main arteries of the extremities by an embolus is not a common occurrence. J. Lerman, F. R. Miller and C. C. Lund (J. A. M. A 94 1128 (Apr 12) 1930) report 6 cases of embolism of the extremities, in 5 of which embolectomy was performed. In 1 case the embolus was located in the axillary artery; in the brachial artery at the profunda branch in another, at the bifurcation of the brachial artery in a third; in the femoral artery at the profunda branch in 2 cases, in 1 of which both femoral arteries were obstructed; and in 1 at the bifurcation of the aorta. In 4 cases cardiovascular disease was the underlying cause of the thrombus; in 1 an aneurism of the subclavian artery; and in 1 case the cause was not definitely established. In cases of this type, the embolus is often palpable as a thickened lump, which usually pulsates vigorously, with transmission of the pulsation for a short distance down the occluded artery.

The success of embolectomy depends on various factors, particularly on the location of the embolus and the time

elapsing between the onset of symptoms and operation. In 2 cases the result of embolectomy was good as far as the circulation of the affected extremity was concerned (1 of the patients died of myocardial disease 13 weeks after operation). The other 3 patients who underwent operation died from 1 to 5 days afterward. The authors emphasize the importance of complete removal of the embolus and the associated thrombus. Irrigation of the occluded artery with salt solution injected at a point distal to the arteriotomy wound establishes the patency of the vessel beyond the point of the original obstruction.

***Sclerosis of Pulmonary Artery.***—

In 3 cases of primary atherosclerosis of the pulmonary artery, reported by S. R. Rosenthal (Arch Path 10:717 (Nov) 1930), cough was the first symptom (The cough was not severe, as the patients mentioned it only after close questioning). Cyanosis was usually the first definite objective sign, present for one or more years before entrance to the hospital. Dyspnea developed soon after cyanosis, though it was not proportional to the depth of cyanosis. Finally, with failure of the right side of the heart, edema developed. A blood count, made in 1 case, showed a true erythemia. All 3 patients were well nourished white men, between 43 and 48 years of age. The occupation of each was associated with aspiration of either particulate matter or gases, which factor seemingly was of pathogenic significance. The characteristic pathologic findings were moderate dilatation of the main trunk of the pulmonary artery (with little or no evidence of atheromatous changes), and definite atheromatous changes beginning in the vessels of the second order of magnitude

and extending to the smaller branches. In every instance the heart was hypertrophied. Microscopically, the changes consisted of, first of all, thickening of the media, the result of an increase of elastic tissue and a hypertrophy of the muscle fibers, later, thickening of the intima develops, and degenerative changes occur in both the media and intima. The lumina of some arteries were found obliterated. These observations seemingly justify primary arteriosclerosis and arteriosclerosis of the lungs as a definite clinical and pathologic entity.

***Thrombosis of Pulmonary Artery.***

—C. H. Boswell and H. D. Palmer (Arch Int Med 47:799 (May) 1931) report a case of fatal pulmonary thrombosis occurring in a shop foreman, 39 years of age. Postmortem examination revealed the pulmonary artery occluded by a well-organized thrombus, in places canalized. The presence of a newer portion of thrombus was evidence that the thrombus had become complete only during the last few hours of life. There was no evidence of chronic congestion, showing that the heart was competent up to the time of the last sudden occlusion; nor was there any sudden pain, as is usual in cases of embolism, and no source of emboli was found. The authors believe that pulmonary thromboarteritis developed by direct extension from a severe respiratory infection, with lymphadenitis and bronchitis, which had been suffered 5 weeks previously. The high coagulability of the venous blood in the pulmonary artery accompanying the sepsis, in addition to a low blood-pressure slowing the blood stream over the damaged artery lining, gave rise to a thrombus which was not extensive enough to cause death at that time. Later, after a good night's rest,

with slowing of the blood stream during sleep, another thrombus formed, and the terminal symptoms appeared with the activity on awakening. Death did not occur until the new portion of thrombus had retrogressed far enough to occlude the larger pulmonary branches.

**Thromboangiitis Obliterans.**—The possibility that thromboangiitis obliterans is an infectious disease is suggested by the work of B. T. Horton and A. H. E. Dorsey (J. Clin. Investigation 10:164 (Apr. 20) 1931). These workers have made bacteriologic studies of acutely inflamed veins and arteries obtained from biopsies or amputations in 34 cases of thromboangiitis obliterans. Pure cultures of Gram-positive pleomorphic streptococci were obtained from 9 cases, and green producing streptococci from 2 cases. Cultures from 24 normal subjects were negative. The organisms isolated have been injected into rabbits and dogs, and pathologic lesions identical to those of thromboangiitis have been produced in a small number of rabbits.

In a study of blood volume by the dye method, S. Silbert, A. L. Kornzweig and M. Friedlander (Arch. Int. Med. 45:948 (June) 1930) found an average reduction of 21 per cent in 69 typical cases of thromboangiitis obliterans, which fact suggests a concentration of the blood in this disease.

**Treatment.**—S. Silbert (J. A. M. A. 94:1730 (May 31) 1930) advocates repeated intravenous injection of **hypertonic salt solution** as an effective and safe treatment in thromboangiitis obliterans. Eighty-four per cent of the patients treated have shown symptomatic improvement, and 67 per cent have been able to return to work. Sixty-four per cent of all ulcers have been healed, and amputation was necessary in

only 8.3 per cent of the patients treated. It is interesting to note that, in an analysis of 460 patients with untreated thromboangiitis obliterans, Silbert found that 64 per cent had an amputation of one extremity during the first 5 years of illness and 46 per cent an amputation of a second extremity during the first 10 years. Silbert is convinced that smoking is the most important contributing factor in producing the disease, and that **cessation of smoking** is an essential therapeutic measure. In his experience, recurrence of symptoms, after the individual had been restored to good condition, has almost invariably been traceable to the resumption of smoking. In a study of basal metabolism, patients with thromboangiitis obliterans showed an average reading of minus 16.2 per cent; men who smoked heavily but were in good health had an average reading of minus 15.1 per cent; and among patients with circulatory impairment due to atherosclerosis, the average reading was plus 9 per cent. This latter study was prompted by the fact that the appearance of patients with thromboangiitis obliterans who have stopped smoking not infrequently suggests a hypothyroid condition. However, no frank instance of myxedema has been observed in a case of thromboangiitis obliterans.

**Shock, Medical.**—The importance of shock as a not uncommon and a very vital complication of certain medical conditions has been emphasized by D. W. Atchley (J. A. M. A. 95:385 (Aug. 9) 1930). Shock, whenever it occurs, is a serious and often fatal condition, characterized by vasomotor collapse, drop in blood-pressure and consequent failure of the circulation. There are 2 types of medical shock, *viz.*, (1) anhydremic shock, dependent on simple



loss of blood volume, an example of which is diabetic coma, and (2) toxic shock, due possibly to capillary paralysis by some bacterial or protein substance, an example of which is vasomotor collapse in pneumonia. In view of the disproportion between blood volume and the vascular bed existing in shock, treatment calls for the following immediate measures to increase the blood volume: (1) First of all, intravenous administration of **hypertonic solution of glucose**, about 50 c c ( $1\frac{1}{2}$  ounces) of a 50 per cent solution, (2) intravenous administration of **physiological saline solution** in 500 to 1000 c c (1 to 2 pints) amounts, and (3) if necessary, **transfusion of blood**. Since heat loss is a contributing factor in shock, **keeping the patient as warm as possible** is most essential, especially in anhydremic shock. From a physiological standpoint, the use of vasoconstrictors, such as epinephrine, is contraindicated, because the blood-vessels which they affect are already constricted to the disadvantage of the capillary circulation.

#### **CORONARY THROMBOSIS.—**

**Incidence.**—During the past few years acute thrombosis of the coronary artery has held a prominent place in medical literature, and, as a consequence, as stated by J B Herrick (*Am Heart J* 6 589 (June) 1931), "the question naturally arises whether the remarkable prevalence is due to an increasing frequency of coronary thrombosis or is merely due to the fact that the condition is better recognized today than formerly." Herrick is of the opinion that possibly modern conditions of living, *i.e.*, "the strenuous life with its speed mania," may be a contributing factor, through its tendency to cause hypertension and arteriosclerosis. Also, today,

more people are reaching adult or senescent years when degenerative vascular changes occur, and, therefore, there are more coronaries to be affected with the lesions that favor thrombosis.

With the exception of cases of embolism and endarteritis obliterans, in almost every instance the ultimate cause of occlusion of a coronary artery is sclerosis of the vessel wall. D. Luten (*Am Heart J* 7 36 (Oct) 1931) states that the causes of arteriosclerosis in general and of coronary sclerosis in particular have not been discovered; however, there are certain secondary factors which frequently contribute to produce coronary thrombosis after sclerosis has been established. The incidence of occlusion does not parallel the extent of coronary sclerosis, many patients with extensive vessel changes never experiencing clinical occlusion; and, on the other hand, occlusion occurs in individuals showing little evidence of coronary disease. Except in rare instances, there is little evidence that infection, either acute or chronic, contributes toward precipitating thrombosis.

Luten points out that there is one striking relationship between coronary thrombosis and angina pectoris, *viz.*, most patients with coronary thrombosis have had attacks of pain conforming more or less typically to angina pectoris. S A. Levine (*Medicine* 8 245 (Sept) 1929), in his splendid monograph on coronary thrombosis, states that the great majority of patients had definite angina pectoris antedating the attack. P D White ("Heart Disease," 411 614, The Macmillan Company, New York, 1931) states that the incidence of occlusion in patients with angina is more than 26 per cent. An-

oxemia of the heart muscle resulting from deficient circulation is looked upon more and more as the basic factor in the production of attacks of angina, though according to T McCrae (Am J M Sc 179 16 (Jan ) 1930), in some cases attacks are seemingly due to causes other than arterial. Pain, therefore, may result from any factor which either increases the need of the heart muscle for blood or diminishes the coronary flow. Also anything which increases coronary flow, but which at the same time increases to a greater extent the demand for oxygen, might also produce pain.

Two possible contributory factors in the producing of thrombosis are (a) a slowing of the coronary flow and (b) a change in the character of the blood. Review of case reports reveals little evidence in support of the latter possibility. A diminution of coronary flow, however, may result from any of the following factors: (a) Lowering of diastolic pressure, (b) lessening of cardiac output, and (c) coronary constriction by vagus stimulation. Striking is the fact that the onset of coronary thrombosis does not attend unusual exertion. In a little more than 40 per cent. of the cases of J Parkinson and D E Bedford (Lancet 1:4 (Jan 7) 1928) the pain began while the patient was asleep or in bed, "often in the early hours of the morning." Seemingly of some significance in this respect is the finding of A. Grollman (Am J. Physiol 95 274 (Nov ) 1930) that the blood-pressure (both systolic and diastolic) and the cardiac output in sleeping subjects falls progressively until about 4 A M. Likewise, the relative frequency of coronary occlusion and thrombosis in the later stages of heart failure is possibly due to the diminished cardiac

output and the enforced rest present in the condition.

Whether or not vasoconstriction is a clinical factor in impeding the coronary circulation is a matter of speculation. The frequent association of gastrointestinal symptoms with angina and coronary thrombosis suggests that gastrointestinal stimuli may precipitate both angina and thrombosis through reflex coronary constriction; however, direct proof of that point is lacking. Other cardiac effects can be so produced, *e g*, J. F. Percy and H. Howard (Am Heart J 2 530 (June) 1927) produced extrasystoles and changes in the ventricular complex in dogs by visceral stimulation. Luten presents 2 cases in which the ingestion of cold fluid seemingly induced coronary occlusion either through a reflex from the stomach or by the direct effect of cold upon the inferior portion of the apex of the heart.

Recent studies of coronary disease have shown not infrequently the existence of a definite familial tendency. J H Musser and J C Barton (Am Heart J 7:45 (Oct) 1931) have advanced the idea that there exist 2 distinct expressions of coronary occlusion. The one is observed in elderly individuals with a well-marked generalized arteriosclerosis, in whom the etiological factors are those of arteriosclerosis in general, representing largely the effects of senescence. The other occurs in men, as a rule, not past the sixth decade of life who do not have generalized arteriosclerosis or hypertension, who have been singularly free from past infections, and who often give a history of coronary occlusion in several members of their family. C F. Coombs (Quart. J. Med 23:233 (Apr.) 1930) states that there are 2 possible inter-

pretations of this familial incidence. One is that it is nothing more than an example of the well-known liability of certain families to arterial degeneration, a liability which in some cases may be general, while in others it may be particular—affecting only certain vessels, such as the cerebral or coronary vessels. Another suggestion is that aberrations of the coronary arteries, throwing an undue responsibility on the one trunk, may run in certain families.

W. D. Stroud (Pennsylvania M. J. 34:469 (Apr) 1931) suggests that individuals born into certain families inherit hyperirritable vasomotor systems, and, therefore, are from birth potential cases of coronary occlusion. The "inherited hyperirritability of the vasomotor system" is analogous to the "spasmogenic aptitude" described by W. R. Houston (M. Clin. North America 12:1285 (Mar) 1929). In such instances, a certain type of environment is the main factor in producing coronary sclerosis with occlusion. These individuals may be identified by taking careful family histories, and the physician can then assist in protecting them from the "necessary environment." It is important, however, to realize the dangers of explaining a possible hereditary factor toward the development of heart disease to a youth with a hyperirritable vasomotor system, since fear and apprehension may hasten the process.

**Symptoms.**—J. B. Herrick (*loc cit*) points out that acute obstruction with its classical picture—"with its severe, enduring substernal or epigastric pain, unprovoked by effort, its attendant shock, lowered blood-pressure, disordered and weakened heart condition, dyspnea, fever, leukocytosis, precordial rub, embolic complications, with death in a few hours or days from ven-

tricular fibrillation or rupture, or with partial or complete recovery after a slow convalescence"—has bulked so large in the consideration of coronary disease that possibly many milder and atypical cases are overlooked. It has been clearly established, for example, that acute obstruction occurs without pain at times. Depending on the size, location and functional importance of the arteries and muscular areas involved, there is every clinical gradation in the severity of symptoms resulting from acute coronary obstruction. The number of cases of heart failure—"insidious, gradual breakdown of the heart's efficiency"—due to slowly progressive obstruction of the coronary arteries is very large. In these latter cases there may be no sudden pain, dyspnea, or drop in blood-pressure. In short, "the coronary artery is a prolific disturber of health."

T. Leary and J. T. Wearn (Am. Heart J. 5:412 (Apr) 1930) report 2 cases of "essential closure" of both coronary orifices. The character of the lesions indicated that closure had been the result of a slowly progressive process which had probably extended over a period of months. Evidence of aortitis was present in each case. Each of the individuals (the one, a Swedish sailor, aged 35 years, the other, a colored dressmaker, aged 26 years) had led an active life to a short time before death occurred suddenly. It is the belief of these authors that the ability of these individuals to live and work was rendered possible through a compensatory circulation supplied by the Thebesian veins, the slowness of the occlusion having allowed time for this readjustment of blood supply.

R. L. Levy (Arch. Int. Med. 47:1 (Jan) 1931) studied carefully clinically a group of 8 cases exemplifying

what appeared to be mild forms of coronary thrombosis. The relative youth of the patients was striking (all being under 50 years of age—the average age, 43 years), as was also the rapid rate of recovery, both subjective and objective. There were 7 males and 1 female, 3 presented a family history of “angina pectoris,” 2, a history of sudden cardiac death in the family, and 1, a family history of hypertension and nephritis. Two had a previous cardiac history of pain on effort, 2, of hypertension; and 1, of a heart murmur following streptococcal sore throat. Six of the 8 patients used tobacco to excess. The 7 men were all engaged in activities calling for driving force, working under pressure; the woman, aged 37 years, was high-strung, the mother of 3 children, an expert equestrienne, and was engaged in directing an amateur theatrical enterprise.

Symptoms of the attack were varied. Substernal pain was the most common complaint, being suffered by 5 patients; vomiting accompanied the attack 3 times; and in 1 case sudden sharp pain in the left arm was the symptom of the onset. Fever, a fall in blood-pressure and leukocytosis were present when looked for. Typical changes in the form of the electrocardiogram were recorded in 6 of the 8 cases.

Of particular significance in characterizing the group of patients was the extraordinarily rapid rate of recovery, as measured by the patient's desire and ability to resume his customary activities, as well as by objective improvement. Even though prostrated by the severity of the symptoms of onset, several of the patients were never truly bedridden, and considered themselves well in from 12 hours to 10 days. To date, 1 of the 8 members of the group has

died of a second, rapidly fatal attack; 1 had a second occlusion 1 year after the first, and a third (the woman) had 2 later attacks. Restoration of function has been complete in 2 cases; 2 others are free from symptoms on restricted activity, and 3 have symptoms (pain over the heart, and dyspnea on exertion) even with carefully regulated lives. The author believes that even though a rapid rate of recovery tends to indicate a favorable outcome of the immediate attack, accurate *prognosis* as to the liability to recurrence and life expectancy is extremely difficult.

**Electrocardiographic Changes in Coronary Artery Disease.**—In an analysis of the electrocardiographic findings in 60 cases of coronary sclerosis, M. H. Nathanson (*Am Heart J* 5:257 (Feb.) 1930) found the most common abnormality to be inversion of the T-wave, which was present in 88 per cent. of the cases. Widened notched QRS occurred in 13.3 per cent. Six cases showed the features of bundle-branch block, 5 of which were such generally accepted as indicating right bundle-branch block, and 1 left bundle-branch block. Minor notching of the QRS complex was not infrequent, and it seemed justifiable to conclude that such notching, especially if present in Leads I and II, is frequently indicative of pathological changes in the myocardium and should arouse suspicion of coronary disease. Electrocardiograms of low voltage were noted in 9 cases (15 per cent.), which is considerably more frequent than the incidence of this deviation in general material. F. A. Willius and W. A. Killins (*Arch. Int. Med.* 40:332 (Sept.) 1927) observed low voltage tracings in but 0.3 per cent. of 140 cases at The Mayo Clinic, 32 per cent. of whom showed evidence of heart dis-

ease Increase in auriculoventricular conduction time was comparatively rare and found only in association with curves of bundle-branch block Arrhythmia of the extrasystolic type was present in 18 per cent of the cases Auricular fibrillation occurred in only 6.6 per cent, all of whom showed evidence of congestive heart failure Curves of left ventricular preponderance were noted in 60 per cent, and of slight right ventricular preponderance in only 3.3 per cent of cases The presence or absence of cardiac enlargement or congestive heart failure seemingly had little effect on the type of electrocardiogram

J B Herrick (*loc cit*) emphasizes the fact that the electrocardiogram in acute coronary thrombosis "registering regressive and reparative processes"—is not fixed but shows variations from day to day or month to month Also it is well to remember that old lesions antedating the present symptoms, or cardiac hypertrophy attendant on hypertension also can give rise to abnormal bizarre tracings; and, therefore, that not all the electrocardiographic abnormalities present in a given case are necessarily due to some recent event suggestive of an acute coronary occlusion In conclusion, he feels that there is no need for further investigation of electrocardiography as related to coronary disease, and that critical reports of carefully worked out single cases may be just as convincing in their conclusions as those based on studies of large series of cases

In a combined electrocardiographic and pathologic study of 47 cases of myocardial infarction, proved by necropsy, A R Barnes and M B Whitten (*Am Heart J.* 5: 142 (Dec) 1929) found the left ventricle involved in every case In 36 cases the infarction was in portions of the left ventricle supplied by the left

coronary artery, and in 22 cases portions of the left ventricle supplied by the right coronary artery were involved Appreciable infarction of the right ventricle was present in only 4 cases, and in each of these instances there was involvement also of the posterior surface of the left ventricle, more extensive than that in the right, but confined to the distribution of the right coronary artery Evidence of infarction did not occur on the anterior surface of the right ventricle in association with occlusion of the anterior descending artery, even though the septum was extremely involved

Occlusion of the left coronary artery usually involved its anterior descending branch, although occasionally the circumflex branch was the site of occlusion In occlusion of the anterior descending branch, infarction at the apex and in variable portions of the anterior portion of the left ventricle and septum was the rule.

The structural differences in the arteries supplying the right and the left ventricles are so striking that seemingly they may play the major part in the localization of coronary infarction M B Whitten (*Arch Int Med* 45: 383 (Mar) 1930) pointed out that the branches of the arteries supplying the right ventricle spread practically in the same plane as that of the artery from which they arise, and that the arteries of the left ventricle leave the main trunks at right angles and penetrate directly through the myocardium It is suggested that the branches leaving at right angles have a tendency to immobilize the larger vessels and thus augment its tortuosities, possibly leading to kinking or constriction, with consequent diminution of its lumen at the point of narrowing

A knowledge of the usual distribution of the coronary arteries is necessary for a consideration of myocardial infarction from a pathological basis

"Both coronary arteries arise from the aorta close to its juncture with the ventricle. The right coronary artery originates from the anterior sinus of Valsalva, and passes to the coronary sulcus. It follows along this groove at the juncture of the right auricle and the right ventricle, and gives off branches to the anterior surface of the right ventricle. One or two of these branches extend anteriorly across the conus arteriosus for about half the distance toward the anterior interventricular sulcus, and they usually end in an anastomosis with similar branches from the anterior descending branch of the left coronary artery. The remaining branches generally parallel one another and pass toward, but do not reach, the apex. At the acute or right margin of the right ventricle a fairly large branch, the right marginal artery and extends down the acute margin about four-fifths of the distance towards the apex.

"The right coronary artery still proceeds in the coronary sulcus and on the posterior surface of the heart gives off one or more branches which may course toward the apex or may go diagonally toward and end in the posterior part of the interventricular septum. When the right coronary artery reaches the posterior interventricular sulcus, it generally gives off a large branch which travels along the sulcus for about three-fifths of the distance from the coronary sulcus to the apex, where it generally turns into the interventricular septum. This branch, which may be called the posterior descending artery, gives off many branches to the posterior third of the septum. The right coronary artery generally continues in the coronary sulcus, crossing the posterior surface of the left ventricle. Here it ends by dividing into two or more branches, which extend from the coronary sulcus for about three-fifths of the distance toward the apex. These vessels usually do not extend to the left beyond a line from one-half to two-thirds of the distance from the posterior interventricular sulcus to the obtuse or left margin of the heart.

"The left coronary artery arises from the left posterior sinus of Valsalva and almost immediately divides into two main branches.

The larger of these branches, the anterior descending artery, proceeds down the anterior interventricular sulcus to the apex, and from this point it generally extends on to the posterior surface of the heart, coursing up the posterior interventricular sulcus usually from a fourth to a third of the distance toward the base of the ventricles. At its termination its branches supply the posterior surface of the apex of both ventricles. As the artery passes down from the anterior surface of the heart, it gives off a few small branches which proceed for a short distance to the right to reach the anterior border of the right ventricle. Several large branches leave the anterior descending artery, passing diagonally downward and to the left to supply the anterior surface of the left ventricle and the lower portion of the obtuse margin. These arteries have been called the accessory anterior descending arteries by Spaltcholz and the rami marginalis by Gross. The anterior descending artery also has many large branches which leave its inferior surface and pass into and supply the anterior two-thirds of the interventricular septum.

"The other main division of the left coronary artery is known as its circumflex branch. It arises near the origin of the left coronary and courses immediately to the left, following the coronary sulcus for a variable distance. It generally passes around the obtuse or left margin of the heart, where it leaves the coronary sulcus to reach and supply the left third or left half of the posterior surface of the basal three-fifths of the left ventricle. Some of the rami marginalis (or accessory anterior descending arteries) may take origin from this vessel instead of from the anterior descending artery.

"In the average normal heart, the left coronary artery supplies the entire anterior surface of the left ventricle, the adjacent third of the anterior surface of the right ventricle, the apex of both ventricles, all of the interventricular septum at the apex, the anterior two-thirds of the remainder of the septum and the left half of the posterior surface of the left ventricle. It also supplies the anterior papillary muscles and the lower portion of the posterior papillary muscles of the left ventricle as well as most of the anterior papillary muscles of the right ventricle.

"The right coronary artery usually supplies two-thirds of the anterior surface and all of



the posterior surface of the right ventricle, except the apex. In addition, it generally supplies the posterior third of the interventricular septum (except at the apex) and the adjacent half of the basal three-fifths of the posterior surface of the left ventricle. The right coronary artery also supplies the posterior papillary muscles, a small portion of the anterior papillary muscles of the right ventricle, and generally the upper portion of the papillary muscles of the left ventricle.

"According to Spalteholz, Banchi (1904) found the coronary arteries to have their average normal distribution, approximately as has been described, in 80 per cent of his 92 cases. However, there are several definite and comparatively common variations from the average distribution of the coronary arteries. The posterior surface of the left ventricle and the posterior part of the interventricular septum are the regions chiefly affected by these variations."

Infarction in the posterior surface of the left ventricle, in the distribution of the right coronary artery, was found to be much more common than had been previously recognized. The fact had never been emphasized that the right coronary artery, where it supplies the left ventricle, has a different type of branching from that in its course in the right ventricle, and, therefore, is especially vulnerable. Also the more frequent incidence of infarction as a result of disease of the anterior descending branch than of the circumflex branch of the left coronary artery might possibly be explained to be due to the fact that the circumflex branch is not anchored so securely by deep branches in its first, or supraventricular, portion as is the entire anterior descending artery.

In a report of 46 cases of *spontaneous cardiac rupture* by E. H. Beresford and C. J. C. Earl (Quart J Med 24:55 (Oct) 1930), recent acute infarction was found to be almost invariably the underlying cause. However, rupture occurs in but 6 per cent of cases of car-

diac infarction. The tear occurs most commonly within the territory of the anterior descending branch of the left coronary artery. The factors which weaken the wall locally are (1) softening, which is practically always associated with excessive mural fat, and (2) intramural hemorrhage. The incidence of rupture increases with advancing years, being highest in the eighth decade. Mental disease was present in 72 per cent of 654 cases reviewed by E. B. Krumbhaar and C. Crowell (Am J M Sc 170:828 (Dec) 1925). The myocardial tear itself is not fatal. Theoretically, death should result from obstruction of the great veins by the raised intrapericardial pressure; however, in some cases but little blood is found in the pericardial sac, which fact suggests that sudden death may be due to a disorder such as ventricular fibrillation.

A. R. Barnes and M. B. Whitten (*loc cit* 1929) found that infarction limited to the anterior portion of the left ventricle, either alone or combined with infarction of the apex, or infarction of the apex alone, produces modifications of the R-T segment of Type T-1\*, whereas infarction of the posterior portion of the left ventricle, with or without infarction of the apex, produces modification of the R-T interval of type T-3\*. Through the characteristic modifications of the R-T and S-T components and of T-waves of the electrocardiogram, these workers believe that it is possible to predict whether the infarction involves the anterior portion of the left ventricle, or the apex, or both, or, on the other hand, the posterior basal portion of the left ventricle and the adjacent interventricular septum.

\* Types T-1 and T-3 were suggested by J. Parkinson and D. E. Bedford (Heart 14:195 (Aug) 1928).

A R Barnes (M Clin North America 14 671 (Nov) 1930) has outlined the electrocardiographic changes to be found in infarction, as follows

I Summary of the electrocardiographic changes involved in infarction of the anterior portion and apex of the left ventricle (commonly due to obstruction of the anterior descending branch of the left coronary artery)

- |  |   |   |
|--|---|---|
| 1 Early stage (1 to 14 days after infarction).     | { | (a) Elevated R-T segment in Lead I and usually in Lead II<br>(b) Rounded, convex or sloping R-T segment in Lead I and usually in Lead II<br>(c) Depressed R-T segment in Lead III   |
| 2 Later stage (14 days to months after infarction) | { | (a) Inverted T wave in Lead I and usually in Lead II<br>(b) Rounded or convex R-T segment in Lead I and usually in Lead II<br>(c) High, positive, sharply-peaked T wave in Lead III |
| 3 Late stage (6 to 24 months after infarction)     | { | Gradual, partial and complete disappearance of the electrocardiographic changes in Stages 1 and 2   |

II Summary of the electrocardiographic changes observed in infarction of the posterior basal portion of the left ventricle and the adjacent interventricular septum (usually due to obstruction of the right coronary artery).

- |  |   |   |
|--|---|---|
| 1 Early stage (1 to 14 days after infarction). | { | (a) Elevated R-T segment in Lead III and usually in Lead II<br>(b) Rounded, convex or sloping R-T segment in Lead III and usually in Lead II<br>(c) Depressed R-T segment in Lead I |
|--|---|---|

- |  |   |   |
|--|---|---|
| 2 Later stage (14 days to months after infarction) | { | (a) Inverted T wave in Lead III and usually in Lead II<br>(b) Rounded or convex R-T segment in Lead III and usually in Lead II<br>(c) High, positive, sharply-peaked T wave in Lead I |
| 3 Late stage (6 to 24 months after infarction)     | { | Gradual, partial and complete disappearance of the electrocardiographic changes in Stages 1 and 2   |

A R Gilchrist and W T Ritchie (Quart J Med 23 273 (Apr) 1930) analyzed the electrocardiographic findings of 148 cases of myocardial infarction reported by various workers. Some degree of *R-T* or *S-T deviation* was found in 52 of 93 cases who had records taken within 10 days of the attack. As first pointed out by Pardce (1920) and later confirmed and amplified by Parkinson and Bedford (1928), this change can be looked upon as strong presumptive evidence of myocardial infarction during the early stages; however, whether positive or negative, it is not an indubitable sign of myocardial infarction. Such change has also been recorded during the course of rheumatic fever, acute rheumatic carditis, pericardial effusion, and lobar pneumonia, and as the result of such factors as changes in the *pH* of the blood, anoxemia, and digitalis therapy. When due to an organic lesion, the presence or absence of this abnormality might be assumed to depend on the particular site or extent of the lesion in the myocardium. Lesions involving the apex of the left ventricle seemingly favor *R-T deviation*. The *T-wave* is the least stable feature of the electrocardiogram, its form, height and direction being influenced by many factors even in health. Exercise,

emotion, heat, cold, various chemical agents, and notably digitalis, are known to affect it. Alteration in the form or direction of T may be a manifestation of slow, progressive myocardial fibrosis due to gradual impairment of blood supply. Also inversion of T in one or more leads may be observed in cases of angina pectoris that have never presented the coronary syndrome, and in patients who have never suffered from cardiac pain. It is well to bear in mind, therefore, that electrocardiographic abnormalities might have been present before the development of thrombosis and infarction. Unlike Barnes and Whitten, these workers concluded that until further evidence has been acquired the form of the electrocardiogram cannot be regarded as a definite localizing sign of the infarct.

With the thought that through frequent electrocardiographic studies, changes might be demonstrated which might not be brought out by single or occasional tracings, W. B. Cooksey and H. A. Freund (*Am Heart J* 6:608 (June) 1931) studied serially 24 consecutive cases of coronary thrombosis. Positive electrocardiographic evidence was found in every case. Aside from the 2 more frequent, commonly mentioned signs, *viz*, deflection of the S-T or R-T interval from the iso-electric level and the cove-shaped negative T wave, the authors emphasize the importance of a marked fall in amplitude of the QRS complex and a flattening out of the T-wave. Coronary occlusion, with subsequent myocardial softening, may well be suspected when the amplitude of the QRS complex becomes diminished in a short space of time. Such change is usually accompanied by a flattening out of the T wave (which often precedes the cove-shaped negative T wave—the

so-called "Pardee T wave of cardiac infarction"). Usually a poor prognosis is indicated where a marked fall of amplitude of the QRS complex either persists or becomes progressively worse beyond the first week or 10 days.

**Prognosis.**—With a growing understanding of the clinical picture of acute coronary occlusion, it has become increasingly evident that a considerable proportion of such patients survive the first attack, and that some thereafter enjoy reasonably good health for a good many years. With the hope of throwing further light upon the fate of such patients who have lived through one attack, L. A. Conner and E. Holt (*Am Heart J* 5:705 (Aug.) 1930) analyzed 287 cases of coronary thrombosis. Approximately 85 per cent of these cases were found in men and 15 per cent in women (which ratio corresponds with that of other statistics). Analysis of the age incidence revealed facts which were both surprising and suggestive. In one-third of all the cases the first attack occurred before the fifty-first year, and in three-fourths of the cases before the sixty-first year. It seems evident, therefore, that coronary thrombosis must be regarded as essentially a disease of early middle life rather than of elderly life, as has been the usual belief.

Evidence of an antecedent arterial hypertension was found in 34 per cent of the cases, of syphilis in 14 per cent, and of diabetes in 10 per cent. The immediate mortality in the first attack was 16.2 per cent, which is surprisingly low [Among Levine's cases (*loc cit.*) the immediate mortality in an attack was 53 per cent, but no statement is made as to the mortality in the first attack alone]. Of 117 patients, who recovered satisfactorily from the first attack, 75 per cent were in good health at the end of the

first year, 56 per cent at the end of 2 years, 21 per cent after 5 years, and 34 per cent after 10 years. One patient remained in good health for 17 years, and died in a second attack 18 years after the first. In 62 per cent of the patients the first attack supervened, without antecedent circulatory symptoms, in persons who had no reason to doubt the integrity of the heart. In 8 out of 22 patients who had antecedent troublesome anginal symptoms and recovered from the first attack of coronary closure, the pain ceased with the attack of thrombosis and did not return, while in 5 patients the pain after thrombosis was worse than beforehand. Only 1 attack of thrombosis was recorded in 67 per cent of all the patients, 2 attacks occurred in 24 per cent, 3 attacks in 4 per cent, and 4 to 7 attacks in 5 per cent. Of the patients having only a single attack, one-half the number were living and one-third were in good health when the authors reported the results of their studies. Among the patients having 2 or more attacks the time interval between the first and second attack was less than 1 year in half of the cases, and in the other half it varied from 1 to 18 years. Signs of arterial embolism appeared 49 times among 42 patients. Twenty-eight of the embolic attacks involved the systemic arteries, and 21 the pulmonary artery.

One hundred and fifty-one of the patients had one or more electrocardiograms which were not at all comparable because in some cases the records were taken only at the time of the acute attack and in others only at some later time. However, changes in T waves (with or without QRS change, not bundle-branch block) were recorded in 109 cases, bundle-branch block in 15 cases; auricular fibrillation or flutter,

transient or permanent, in 19 cases, and heart-block, complete, 21 or dropped beats, in 7 cases.

Although the immediate mortality was higher when the initial symptoms were severe, it was found that almost one-third of the patients who recovered from the attack had had symptoms of very severe character.

In a series of 200 cases of coronary thrombosis studied by P. D. White and E. F. Bland (*Am Heart J* 7.1 (Oct) 1931), 101 died on an average of 15 years after the attack. The average duration of life to the time their study was reported for the entire series of 200 patients was 24 years. The patients who died almost always succumbed to either congestive heart failure, angina pectoris or a subsequent coronary occlusion. The younger patients, as a rule, lived a little longer. Sex appeared to be unimportant. Neither the previous occurrence of angina pectoris nor its duration prior to the attack of coronary thrombosis seemed to matter. The presence of hypertension was not important, and syphilis was rarely encountered. Cardiac enlargement of considerable degree was found to be a somewhat unfavorable sign, and the presence of congestive failure and poor heart sounds added considerably to the gravity of the prognosis. Good treatment seemingly influenced the prognosis. Treatment, consisting primarily of rest with long convalescence and a careful life afterward, had generally been much better carried out in the patients who survived than in those who died.

*Sedimentation Time*—M. A. Rabinowitz, C. Shookhoff and A. H. Douglas (*Am Heart J* 7.52 (Oct.) 1931) found definite shortening of the red cell sedimentation time in 10 cases presenting the clinical picture of acute coronary

occlusion This change appeared later than the fever and leukocytosis, and persisted for some time after the temperature and blood count had returned to normal They suggest the advisability of keeping a patient with coronary occlusion in bed for at least as long as the sedimentation time points to active myocardial changes (*i e*, as long as it is below 60 minutes)

**Treatment.**—R L Levy and A L Barach (J A M A 94 1363 (May 3) 1930) report favorable results from the administration of oxygen in a concentration of from 45 to 50 per cent. in the treatment of acute coronary thrombosis Subjective improvement, manifesting itself chiefly by relief of respiratory embarrassment and restlessness, occurred in from 1 to 2 hours after the administration of oxygen was begun Cyanosis was diminished or abolished, the respiratory rate was lowered, Cheyne-Stokes respiration, if present, tended to disappear, the heart rate became slower, and the heart sounds grew stronger and the volume of the pulse improved In 2 cases the oxygen tent was employed continuously for 1 week and at intervals for 2 weeks more The authors firmly believe that the effective use of oxygen may prove a life-saving measure in some cases

#### ELECTROCARDIOGRAPHY.\*—

**Significance of Axis Deviation.**—Considerable discussion centers about the significance of axis deviation In a study of the essentially normal heart of a young man upon whom a pericardiostomy had been performed for suppurative pericarditis, P. S. Barker, A. G. Macleod and J. Alexander (Am Heart J. 5:720 (Aug) 1930) found that the excitation process appeared

earliest on the anterior surface of the right ventricle near the atrioventricular borders (which suggests that the conducting tracts in the right ventricle of man differ from those of the dog). By studying the curves produced by stimulating various points on the surface of the heart, as recorded in the 3 standard leads of the electrocardiogram, it was found that ventricular premature contractions of right ventricular origin are represented in the electrocardiogram by ventricular complexes in which the chief initial deflection is upward in Lead I; and ventricular premature contractions of left ventricular origin are represented in the electrocardiogram by ventricular complexes in which the chief initial deflection is downward in Lead I. It is suggested, therefore, that the clinical electrocardiograms at present ascribed to block in the right branch of the His-bundle indicate block in the left branch, and *vice versa*, and that in so-called left ventricular preponderance, the electrocardiogram is dominated by right ventricular effects, and *vice versa*. [This conclusion, if accepted, would involve more than a mere change in electrocardiographic nomenclature; it is in conflict with the prevailing views regarding the origin of the initial ventricular deflections of the normal electrocardiogram, and of those curves now attributed to preponderant hypertrophy of the one or the other ventricle—as originally advanced by Lewis]

On the other hand, in a study of 334 cases in which the electrical axis was compared with orthodiagrams and clinical observations, S. H. Proger and D. Davis (Arch Int. Med 45:974 (June) 1930) found that clinical conditions generally associated with left ventricular preponderance tend to produce left axis deviation, and that those associated

\* See also Cardiac Arrhythmias

with right ventricular preponderance more constantly produce right deviation. This relationship is presented more regularly in enlarged hearts than in hearts of normal size. In the normal hearts, no constant relationship was noted between the electrical axis and transverse position of the heart. All the hearts with right axis deviation presented either mitral stenosis, congenital heart disease, or chronic emphysema.

***Electrocardiogram in Obesity.***—

In a study of 55 cases of simple obesity, without evidence of cardiac enlargement or hypertension, S. H. Proger (Arch. Int. Med. 47:64 (Jan.) 1931) found definite left axis deviation in 31 (56 per cent), inversion of the T-wave in Lead III in 39 (71 per cent), and flat or inverted P-waves in Lead III in 24 cases. Proger believes that left axis deviation due to change in position of the heart is usually associated with inversion of the T-wave in Lead III, while left axis deviation due to left ventricular hypertrophy is commonly associated with an erect T-wave in Lead III. On comparing these electrocardiograms with those of 40 cases of obesity with cardiac complications and 5 cases of essential hypertension without demonstrable cardiac involvement, it was found that the electrical axis did not differ materially whether or not the heart was involved. The author concludes, therefore, that axis deviation in the obese patient is of no value as an aid in the diagnosis of relative ventricular hypertrophy.

***Low-voltage T-waves.***—A. M. Master (Am. J. M. Sc. 181:211 (Feb.) 1931) has studied a series of 107 cases having an amplitude of not more than 1 mm. in any lead. Postmortem examination was made in 12 cases, and every one showed definite changes in the myocardium or the pericardium. Of 12

other cases who died, 11 had myocardial failure and 1 pulmonary tuberculosis. Acute rheumatic infection of the myocardium or pericardium often produces a flat T-wave, and in the progression of the disease it may become inverted, or with the patient's recovery it will become upright. It may also occur in pneumonia, bronchitis, pleurisy with effusion, or severe hyperthyroidism. The so-called "coronary T-wave" or "cove-plane T-wave" may appear in rheumatic pericarditis. In a series of 18 ambulatory patients with flat T-waves almost 90 per cent had degenerative cardiovascular disease.

***Large Q-wave in Lead III.***—H. E. B. Pardee (Arch. Int. Med. 46:470 (Sept.) 1930) after a series of careful observations, reports that the majority of the electrocardiograms showing large Q-waves in Lead III are obtained from patients presenting the anginal syndrome (being found in 8 (27 per cent) of 33 cases of this type studied). J. Parkinson and D. E. Bedford (Heart 14:195 (Aug.) 1928) found a large Q-3 in 9 (31 per cent) of 29 patients with coronary thrombosis. This abnormality may also be presented by certain patients with myocardial fibrosis and congestive heart failure, rheumatic heart disease (especially with pericarditis), and at times in hypertension. It was found only twice among 277 individuals with apparently normal hearts. Its occasional presence in normal hearts may be due to an unusual distribution of the branches of the auriculoventricular bundle, and also a high position of the diaphragmatic movements on the large Q-wave, it being present in forced expiration and absent in forced inspiration. The author suggests that the presence of a large Q-3 is indicative of disease of the left ventricle.



In a study of 300 cases with large Q-waves in Lead III of the electrocardiogram reported by F A Willius (Am Heart J 6 723 (Aug) 1931), 89.3 per cent of the records were obtained from patients with one of the following conditions: hypertensive heart disease, the anginal syndrome, hypertensive heart disease accompanied by the anginal syndrome or hypertension. The majority of the remaining 32 patients (10.7 per cent) had diseases that exert an influence chiefly on the left ventricle. The dominant condition in which this abnormality occurs is hypertensive heart disease.

**Changes in Scarlet Fever and Diphtheria.**—In an attempt to show that the electrocardiographic changes occurring in rheumatic fever are non-specific, C Shookhoff and L M Taran (Am. Heart J 6 541 (Apr) 1931) studied 50 children with diphtheria and a similar number with scarlet fever. (The chief electrocardiographic abnormalities in rheumatic fever, as discussed by various writers, consist of: (1) Changes in rate and rhythm; (2) changes in the auriculoventricular conduction time, from a slight prolongation to the higher degrees of heart-block; (3) changes in the ventricular portion of the electrocardiogram, involving abnormalities in position and shape of the S-T or R-T interval, height and direction of the T-wave, and height and shape of the main deflection.) In comparison with the findings in rheumatic fever, the scarlet fever patients showed an absence of conduction disturbances, a comparative infrequency of abnormalities of the ventricular portion of the electrocardiogram, and a complete clearing up of these abnormalities early in convalescence. The abnormalities found in the diphtheria group resembled more

closely those described in rheumatic fever, in that they occurred in a high percentage of children suffering from only a very mild infection, that the changes had a tendency to persist, and that they might be found when no clinical signs of myocardial involvement are present. The absence of auriculoventricular conduction disturbances in the milder cases of diphtheria was, however, striking.

**Diphtheria and Late Heart-block.**

—S Butler and S A Levine (Am Heart J 5 592 (June) 1930) studied a group of 20 patients with heart-block without the customary causes, such as rheumatic infection, arteriosclerosis, syphilis, digitalis and fever, to determine the incidence of diphtheria in childhood. The incidence was 50 per cent as compared to 6 per cent in a control group of 600 consecutive surgical cases. Striking is the fact that the average age of the patients with a positive diphtheria history was 11 years younger, and their systolic blood-pressure 40 mm lower than in those with a negative diphtheria history. This study suggests that, after a variable latent period (of even several or more decades), diphtheria in some way either brings about impairment in the conduction system causing heart-block, or predisposes the heart to sclerosis which in the absence of diphtheria would have matured at a later age.

**Changes in Pneumonia.**—In a study of 45 patients with lobar pneumonia and 7 with bronchopneumonia, A M. Master, A Romanoff and H. Jaffe (Am Heart J 6 696 (June) 1931) found a definite increase of the auriculoventricular conduction time, ranging from 0.20 to 0.24 seconds, in 35 per cent. This change occurred when the temperature became normal in the be-

gining of convalescence, and was affected but slightly with atropine sulphate. R-T abnormalities occurred in 93 per cent of the cases of lobar pneumonia, also appearing with the fall of temperature to the normal level. These deviations were similar to those observed in coronary occlusion, but did not progress to an inverted T-wave. The fatal cases showed marked tachycardia, a large number of T-wave inversions (44 per cent), and an absence of auriculoventricular conduction impairment, bradycardia, sinus arrhythmia, and large T-waves. The authors believe that the electrocardiographic changes are the result of toxicity associated with the disease. Some degree of parenchymatous degeneration of the heart muscle was seen in postmortem examinations of 8 of 9 fatal cases.

#### **HYPERTENSION.—*Etiology.*—**

In a study of the circulatory mechanism in hypertension, S. Weiss and L. B. Ellis (*Am Heart J.* 5:448 (Apr) 1930) found that, even though the average resistance of the arteriolar system of the greater circulation is twice as great as in normal control subjects, the circulating blood volume, the cardiac output per minute, and the mean velocity of the circulation are either normal or slightly below normal. These findings confirm their previous work (*J. Clin Investigation* 8:47 (Dec) 1929), in which the capillary pressure in hypertensive patients was found to differ but little from that of normal controls. They believe that hypertension might be a compensatory phenomenon designed to maintain normal tissue oxidation through a normal capillary blood flow.

E. J. Stieglitz (*J. A. M. A.* 95:842 (Sept 20) 1930) states that anything that irritates the arteriolar musculature or stimulates the sympathetic pressor

fibers may represent the original cause of hypertensive vascular disease. Some of the commonly known irritants—"initiating factors"—are endocrine disturbances, dietary irritants, infections, intoxications with metals or chemical irritants, anemia and predisposition to early fatigue of the vascular structures. E. J. Stieglitz ("*Arterial Hypertension*," Paul B. Hoeber, New York, 1930). The perpetuating factor is the vicious circle of spasticity causing muscular fatigue, the fatigue leading to increase of arteriolar irritability, and in turn more spasticity and fatigue. This process, if not checked, leads on to degeneration of the hypertrophied arterial muscle, with subsequent fibrous tissue replacement and arteriolar sclerosis—which later stages are not reversible.

In an analysis of 500 cases of arterial hypertension, F. R. Nuzum and A. H. Elliot (*Am J. M. Sc.* 181:630 (May) 1931) found past infections to be of slightly more frequent occurrence in the hypertensive group than in a control group of 250 patients of similar age with an average systolic pressure of 120 mm. of mercury. Acute nephritis and scarlet fever occurred more frequently in a subgroup of 70 patients with chronic nephritis than in the other hypertensive individuals and the controls. The number of past infections per patient was almost identical in each group. The incidence of syphilis and typhoid fever was lower than generally reported in hypertension. Focal infection was seemingly not the deciding factor in the development of hypertension, being almost evenly distributed among the groups. Obesity was encountered twice as often in the hypertensive group as in the controls. The average weight in the hypertensive group was 10.3 pounds greater than that of the controls. No

striking familial tendency to hypertension was noted, a positive history of familial vascular disease being obtained in about 30 per cent in both groups. In as much as palpable or ophthalmoscopic evidence of arteriosclerosis was found in 17.6 per cent of the main hypertensive group, in 24.2 per cent. of the nephritic group, and in 14.4 per cent of the control group, it was concluded that arteriosclerosis of the larger vessels probably has little relation to hypertension.

N. M. Keith, N. W. Barker and J. W. Kernohan (Tr. A. Am. Physicians 46:66, 1931) studied the arterioles in sections of the pectoralis major muscle obtained from 143 living patients suffering from hypertension. Definite changes were found in the small arteries and arterioles, ranging from increased prominence and tortuosity, with increase in the number of medial and intimal nuclei, to thickening of the walls, with definite increase in the ratio of the thickness of the wall to the diameter of the lumen. The changes occurred more often in cases of severe hypertension, but were not proportional to the duration, height or fixation of the blood-pressure. With arteriolar changes and a clinical picture indicating diffuse arterial disease, the ultimate prognosis was serious.

**Symptomatology.**—In a study of the symptoms associated with essential hypertension and those of the psychoneuroses, D. Ayman and J. H. Pratt (Arch. Int. Med. 47:675 (May) 1931) found that the early symptoms in the 2 conditions could not be differentiated, that in both groups emotional difficulties, sufficient to explain the symptoms, were present at the time the symptoms appeared. Additional evidence that the early symptoms in emotional hypertension are not due to organic changes but to emotional maladaptation is suggested

by the results of treatment (D. Ayman: J. A. M. A. 95:246 (July 26) 1930). The authors believe that constitutional influences, endocrine products, and possibly other factors, may contribute to lessen the hypertensive patient's psychic and physical capacity for withstanding the stress and strain of life.

In an analysis of the complaints of 1090 ambulatory patients with primary (essential) hypertension, J. E. F. Rise-man and S. Weiss (Am. J. M. Sc. 180:47 (July) 1930) concluded that arterial hypertension is not associated with characteristic symptomatology. Almost all the symptoms of hypertensive patients are believed referable to a disturbance of the central nervous system and are expressions of a disordered vasomotor system. Headache was a symptom in 43.3 per cent, dizziness in 40.3 per cent, "aches and pains" in 38.7 per cent, dyspnea in 27.7 per cent, and nycturia in 25.9 per cent of the cases. Epistaxis and migraine were infrequent symptoms. Attention is called to the fact that certain conditions with normal blood-pressure, *viz.*, menopause, obesity and psychoneurosis, at times show symptoms similar to arterial hypertension, and that frequently in all 4 conditions vasomotor instability is exhibited. It is concluded, therefore, that psychic conditions may play an important rôle in hypertension, and deserve consideration in the treatment of the condition.

D. Ayman (J. A. M. A. 94:1214 (Apr. 19) 1930) warns against the physician's being satisfied with a normal blood-pressure reading at one visit when there is reason to suspect hypertension. The possibility of hypertension may be suggested by symptoms, such as, dizziness, headache, rheumatoid pains, irritability, palpitation, a sensation of weight in the chest, mild fatigue, and

sexual impotence. Normal blood-pressure readings were observed on one or more visits of 43 (56 per cent) of 76 unselected, untreated hypertensive patients. The patients whose blood-pressure dropped to normal at least once were on the average 9 years younger than the group of 33 patients whose blood-pressure remained persistently above normal. Cardiac enlargement was present in only 6 of the 43 patients with wide blood-pressure variations. At times, it is difficult to separate emotional hypertension from essential hypertension.

Fluctuation of the diastolic pressure over a wide range was observed by D. Ayman (Arch Int Med 48:89 (July) 1931) in all of 76 untreated patients with essential hypertension. No appreciable difference was found between patients with severe hypertension and those with milder forms. The percentage of diastolic fluctuation was as great as that of the systolic pressure. Sitting in a quiet room had a definite lowering effect, and excitement had an elevating effect.

**Incidence and Prognosis.**—J. M. Blackford, J. M. Bowers and J. W. Baker (J A M A 94:328 (Feb. 1) 1930) obtained family histories of hypertension in more than one-third of the histories of 401 hypertensive patients (systolic pressure 175 mm or over) found in 10,000 examinations in a general clinic. Hypertension was found to occur in middle life (past 50 years) in 16 per cent of patients seen in general practice. After being established, no tendency toward recovery was observed. It occurs twice as frequently in females; but the female mortality averages only half that among males (as shown by records in a 5-year follow-up study). Terminal failure of the renal system as

a cause of death was noted in a relatively small percentage of the patients compared with deaths due to changes in the cerebral or coronary vascular systems.

According to E. J. Stieglitz (Arch Int Med 46:227 (Aug) 1930), the prognosis in arterial hypertension depends largely on the extent of irreparable, permanent vascular and cardiac injury. Spasticity and hypertonicity, no matter how severe, are amenable to therapy, but degeneration of muscle cells and replacement with fibrous tissue represent permanent injury—not amenable to treatment. He recommends the inhalation of amyl nitrite to determine the degree of vascular relaxability, and, thereby, aid in the evaluation of the prognosis in hypertension. The age of the patient and the severity of hypertension *per se* are not factors of any moment. However, persistence of diastolic hypertension is significant. If the diastolic pressure is maintained at 135 mm. or higher, renal involvement is to be expected, and the outlook is very dubious. The degree of variability in the height of the diastolic tension constitutes an effective criterion of the extent of irrevocable arteriolar changes.

D. Riesman (J A M A 96:1105 (Apr 4) 1931) points out that hypertension, while occasionally transitory, is usually a permanent and progressive condition. (More or less transitory states of hypertension may be due to emotion, to physical exertion, to hypertrophy of the prostate, and rarely to suprarenal tumors—disappearing with removal of the cause.) He looks upon hypertension as a disease of American life, its causes being connected with the striving for wealth, stating: "We have created false standards, have deprived ourselves of peace and leisure, and have

lost the art of living wisely." Though high blood-pressure is not conducive to longevity, he believes it is, nevertheless, compatible with longevity. As an example, is cited a female patient, aged 97 years, whose clinical course he has followed for more than 25 years, during which period her systolic pressure ranged from 220 to 274, with a diastolic pressure always about 100. In foretelling the future of the hypertensive individual, the following points deserve consideration. (1) Old persons bear high blood-pressure better than younger ones, (2) the height of the blood-pressure, unless excessive, is not in itself a reliable criterion; (3) a high diastolic pressure is a bad prognostic sign (indicating the steady, irreducible minimum load against which the heart must work), (4) the outlook in uncomplicated hypertension is better in members of long-lived families (since longevity is largely an inherited trait), (5) irascibility is not conducive to longevity in the face of hypertension, (6) the state of the arteries, the eye-grounds, the size of the heart, kidney function, and the coexistence of diabetes have a definite influence on prognosis.

**Treatment.**—The successful treatment of essential hypertension by different drugs and methods of treatment has been reported at least 200 times in the last decade, according to D. Ayman (J. A. M. A. 95:246 (July 26) 1930). The salient features of 35 unselected articles are summarized by Ayman, as follows. (1) In practically every article, complete or partial symptomatic relief is reported; (2) in the majority of the papers, a moderate reduction in blood-pressure is reported; occasionally there is a marked reduction, (3) the degree of symptomatic relief is generally greater

than the degree of blood-pressure reduction (but in many instances the blood-pressure drops are only 20 or 30 mm, which are impossible to distinguish from the spontaneous variations so characteristic of the untreated disease); (4) the degree of symptomatic relief is frequently out of all proportion to the reduction in blood-pressure; (5) marked symptomatic relief sometimes occurs without any reduction in blood-pressure, (6) complete failure is seldom reported. On the basis of these reports, Ayman concluded that there is a common and specific factor associated with the administration of most of the drugs used, *viz*, "treatment"—consisting of the enthusiastic giving or doing of something to the patient—regardless of its nature. Accordingly, to an unselected group of 40 hypertensive patients with active symptoms, 10 drops of **dilute hydrochloric acid** in a half-glass of water 15 minutes before meals, 3 times daily, was prescribed "seriously and enthusiastically." Definite symptomatic relief occurred in 33 cases (82 per cent)—the majority feeling better after 1 week. The author concludes that the symptoms of essential hypertension are frequently of psychic origin, and, therefore, may often be relieved by the suggestion inherent in any drug or method employed by the physician.

**Bismuth Subnitrate**—E. J. Stieglitz (J. A. M. A. 95:842 (Sept 20) 1930) reports a fall in the diastolic pressure to 100 mm or below in 77 per cent of 200 unselected cases of arterial hypertension treated with bismuth subnitrate (prescribed in capsules of 10 grains (0.6 Gm) *t i d*). It is assumed that bismuth subnitrate is slowly decomposed in the bowel, liberating nitrate ions which are reduced by *Bacillus coli* to nitrous acid; and thus minute quantities

of nitrite ions are continuously absorbed, effecting gradual persistent vascular relaxation and reduction of the arterial tension (Small amounts of nitrite ions are detectable in the urine during this therapy) In hypertension in pregnancy, if the intoxication is not too profound, a moderate fall in tension is obtainable Anticipation of good results is not justified in cases in which actively operating etiologic factors, such as oral sepsis or grossly injurious dietary habits, are neglected Furthermore, marked impairment of renal efficiency inhibits good results, and extensive arteriolar sclerosis precludes any extensive improvement

*Cucurbitacin* — The use of cucurbitacin (watermelon-seed extract) has been recommended by several writers for the relief of hypertension S L Gargill and A Rudy (Am J M. Sc 181 639 (May) 1931), on the other hand, were not convinced of its efficacy in a study of a series of 29 patients The drug was administered by mouth in capsules containing 50 mg ( $\frac{5}{16}$  grain) of the glucoside The majority of the patients were given 300 mg. (5 Gm) daily, and most of them were treated for 2 to 3 months. Only 7 (24 per cent) showed a reduction in systolic pressure of 25 mm or more of mercury; and in only 2 instances was there complete symptomatic relief The spontaneous variability of the blood-pressure in patients with arterial hypertension is discussed, and its importance in the evaluation of therapeutic results is emphasized

*Thiocyanates* — Somewhat conflicting reports regarding the value of the thiocyanates in the treatment of essential hypertension have been published, however, most writers agree that there are certain objectionable features and limi-

tations attached to this therapy J F Borg (Minnesota Med 13 293 (May) 1930) emphasizes the fact that while the sulphocyanates are efficient drugs in the treatment of hypertension, the possibility of unpleasant side effects must be borne in mind, and, therefore, the drug should only be employed when the patient is under close observation Side effects manifest themselves commonly in weakness and in dizziness, but may progress to a psychotic state with disorientation, hallucinations of sight and hearing, ideas of persecution and mania

M H Fineberg (J. A. M. A. 94 1822 (June 7) 1930) reports that 22 (37 per cent) of 58 hypertensive patients treated with sedatives, either sodium bromide (15 grains—1 Gm, *t. i. d.*) or phenobarbital ( $\frac{1}{4}$  to  $\frac{1}{2}$  grain—0.016 to 0.03 Gm, *t. i. d.*), over a 3 months' period showed a sustained drop of 30 mm or more in blood-pressure, with definite symptomatic improvement and that symptomatic relief was experienced by others without a drop in blood-pressure. Of 13 of these patients who were then given potassium thiocyanate in doses of  $1\frac{1}{2}$  grains (0.1 Gm) 3 times a day and followed for another 3 months' period, only 1 showed a definite lowering of blood-pressure (the systolic pressure dropping from 164 to 138 and the diastolic from 98 to 82). Twelve (57 per cent.) of 22 patients who were given potassium thiocyanate in dosage of approximately 5 grains (0.3 Gm.) 3 times a day showed a fall in systolic pressure of 30 mm or more. No harmful effects were observed in any of the patients given the small or the large doses. In final analysis, subjective improvement was greater attending the use of the sedatives, while the lowering of blood-pressure was more marked with the heavier doses of thiocyanate.



After a review of the literature, D Ayman (J A M A 96 1852 (May 30) 1931) states that there is no clear evidence to show the clinical value of the thiocyanates in essential hypertension. He points out that a simultaneous toxic effect is almost always associated with the hypotensive effect, which effects are produced either by large doses given for short periods or by small doses for long periods. His studies point to the impracticability of potassium thiocyanate therapy at least in patients presenting narrowing of the retinal arterioles, cardiac enlargement, or renal involvement.

**CARDIAC NEUROSES.**—L. A. Conner (J A M A. 94. 447 (Feb. 15) 1930) states that the *psychic factor* in cardiac disorders is deserving of consideration for the following reasons: (1) The great prevalence of cardiac disorders having as their chief or only determining cause some purely emotional disturbance; (2) the frequency with which such psychic disturbances are the result of some injudicious statement or action on the part of a physician; (3) emotional reactions may play a very important part in the clinical picture in patients with unmistakable evidence of organic heart disease, and (4) the necessity for the practitioner to have a full and sympathetic understanding of these psychic factors for successful treatment.

Neuroses may be classified as (*a*) the psychoneuroses—made up of morbid fears, apprehensions, anxieties, indecisions and depressions, and (*b*) the so-called organ or the vegetative neuroses in which the symptoms are due to disturbance of the functions of one or more of the internal organs. The psychic reaction to doubt concerning the integrity of the heart seems to be much more violent and profound than is the

case with any of the other organs. In the minds of most laymen the thought of heart disease is still associated with the idea of sudden and unforeseen death. The normal functioning of the organs under the control of the vegetative nervous system is maintained through a fine balance between the accelerator and inhibitory mechanism, without participation of the conscious mind; however, all these functions are to some degree susceptible to psychic influence. Transient disturbance of this equilibrium occurs in normal individuals as a reaction to sudden psychic stimulation; but in the "neurotic" individual this response of the vegetative nervous system seems grossly exaggerated and out of all proportion, in its severity or in its duration, to the psychogenic stimulus. Though a careful search may fail to reveal a direct and obvious relationship between cardiac symptoms and some definite psychic disturbance, it rarely fails to disclose evidences of some instability of the nervous system as it relates either to the mind or to the autonomic system, such as history of a "nervous breakdown," exaggerated introspection, morbid concern for health, great suggestibility, or clinical evidences of a disturbed autonomic nervous mechanism—such as instability of vasomotor control, extreme lability of the pulse rate or blood-pressure level, or marked sinus arrhythmia.

The psychogenic stimulus usually arises from one of the following causes. (1) The statement of some physician that the heart shows some abnormality, such as a murmur or an irregular rhythm; (2) the occurrence of some dramatic case of heart disease among relatives or friends; (3) the appearance of some symptom referable to the heart leading to a doubt of its integrity; (4)

some profound and protracted emotional disturbance, such as deep grief or prolonged anxiety, without any doubt at first regarding the heart (In group (4) belong the cases of neurocirculatory asthenia, known also as "the effort syndrome" or "the irritable heart of soldiers")

**Symptoms.**—Symptoms are usually subjective in character, including every possible variety of sensation ranging from slight fulness, soreness or "pressure," to severe anginal pain radiating to the arm, neck or back, palpitation, fluttering, pounding or throbbing in the ears or temples, a sensation as though the heart were not beating, the inability to take a satisfactory breath, without any actual dyspnea even on exertion

**Pain**—Pain, when present, differs from true anginal pain, rarely being referred directly to the retrosternal region, usually being located at the apical region or over the left half of the precordium, consisting of twinges of darting pain. It is usually felt during repose, rarely being associated with effort. At times, however, the pain is such that it is extremely difficult to rule out coronary artery disease

**Objective Signs**—Tachycardia in response to any emotional disturbance is especially common, not infrequently accompanied by throbbing of the whole precordium. Undoubtedly, pronounced slowing occurs in some cases. Ventricular premature beats, even without the influence of toxic agents such as tobacco and coffee, are frequently presented. Excessive vasomotor instability, evidenced in the form of ready flushing to slight emotional changes, is seen in most patients.

**Psychic Factor in Organic Heart Disease.**—Individuals with organic heart disease may possess mental make-

ups which predispose them to apprehensions and fears, and, as a consequence, there may be symptoms not reasonably ascribable to the organic disease present. In these cases the proper evaluation of the symptoms demands the utmost in skill, judgment and experience on the part of the physician. At times, profound and protracted emotional disturbances play a part in aggravating the existing heart damage and in producing serious cardiac symptoms. Physicians are much too prone to fail to give proper weight to the potentialities for harm present in violent psychic stimuli

**Treatment.**—Treatment of the psychic aspects of cardiac disorders calls for experience and sympathetic insight into the processes of the human mind. In many instances, the problem is simple, a tactful explanation of the situation and reassurance being all that is needed, and at other times the problem calls for the assistance of an experienced psychiatrist. As a prophylactic measure, the physician should exercise great care to avoid supplying the unstable patient with a cardiac neurosis through any suggestion that may serve to crystallize fluid anxieties and center them on the heart. If an unimportant cardiac anomaly is noted in the course of a health or insurance examination, it is often wise not to mention it; but, if it seems necessary to apprise the patient the matter should be presented with sufficient reassurance to put his or her mind at rest regarding its significance. Anxious parents of children with mild forms of heart disease should not be unduly alarmed.

The patient should be informed that the symptoms are due to emotional causes rather than to disease of the heart itself. However, the patient

should not be allowed to interpret this as meaning that the symptoms are "imaginary," since the first reaction to such a disclosure is apt to be strong resentment. The patient should be convinced that the pain, palpitation and dyspnea are no less real and disturbing because due to agencies outside the heart, but that in this case the symptoms are curable. This should be preceded by a thorough physical examination, since a superficial examination will fail to carry conviction.

The promptness and completeness of recovery are dependent on the skillful application of **reassurance** and **encouragement**. However, the patient must be shown that his cardiac symptoms are improved rather than made worse after exercise and effort which previously he may have feared to undertake. **Exercise** serves the double purpose of demonstrating to the patient that his heart is capable of much more than he supposed and of rendering the heart less irritable and less ready to respond to psychic stimuli. The form of exercise will vary with the individual patient.

Drugs should be avoided unless absolutely necessary. At first, perhaps, the sedative action of **bromides** and **phenobarbital** may be indicated, but they should be discontinued as soon as the urgent need for them has passed. Digitalis and quinidine should be avoided. The advisability of rest in bed, baths and massage depends upon the probable effect of such measures on the patient's mind. The chief objection to them is that they serve as a constant reminder that he is not well, which mental effect will counteract any possible benefit. As to smoking and coffee drinking, it is usually wise to permit the habit within bounds.

**ORTHOPNEA.**—A new hypothesis to explain the mechanism of orthopnea in uncomplicated *myocardial failure* of the congestive type has been proposed by A. C. Ernstene and H. L. Blumgart (Arch Int Med 45: 593 (Apr) 1930). The hypothesis is based on the fact that increased cerebral venous pressure diminishes intracranial blood flow, thereby favoring increased anoxemia of the respiratory center. Accordingly, the patient suffering myocardial failure and increased venous pressure always tends to maintain an elevation in bed sufficient to keep the respiratory center above the top of the pressure column of venous blood extending upward from the right auricle. In the upright position the pressure in the veins about the respiratory center is kept more nearly normal than in any other position, and the blood flow in the capillaries feeding these veins is increased to the maximal limit permitted by the existing myocardial failure. The validity of the hypothesis was tested by making comparisons of the height of the venous pressure and the degree of orthopnea in 22 patients with uncomplicated myocardial failure of the congestive type. A definite parallelism between the 2 measurements was observed. In general, the higher the venous pressure, the greater was the degree of orthopnea. An observation which strongly supported their theory was that when orthopneic patients were placed in the recumbent position with the head flat, simple elevation of the head by flexion of it on the thorax produced, almost without exception, conspicuous diminution of respiratory distress. This procedure favors diminution of the cerebral venous pressure, but has no significant effect on the vital capacity of the lungs. These workers believe that, although various factors

contribute to the relief experienced in the sitting position, the relatively low cerebral venous pressure in the upright posture is the primary factor in reducing the respiratory discomfort in patients with congestive heart failure and increased venous pressure.

**PATHOLOGY.—Beriberi.**—In a study of 15 patients with cardiac insufficiency due to beriberi, C S Keefe (Arch Int. Med. 45:1 (Jan) 1930) found enlargement of the heart in all cases, due principally to increase in size of the right auricle and right ventricle. Another striking feature was an increase in the x-ray shadow in the region of the pulmonary artery and the superior vena cava. With rest in bed and an anti-beriberi diet supplemented with yeast, the teleroentgenograms showed the size of the heart to decrease in a short time, the patient becoming normal. The study also showed that the beriberi patients who develop cardiac insufficiency are the ones who have the least involvement of the nervous system. It is concluded that muscular exercise plays a great rôle in the course of the disease. If the patient is not disabled by polyneuritis and performs muscular work, cardiac insufficiency results, while, in other instances, where polyneuritis is present, the myocardium is usually protected from the burden of muscular exercise and cardiac failure does not appear. Cardiac insufficiency is seemingly due to a deficiency of vitamin B which causes changes in the myocardium.

**Subacute Bacterial Endocarditis.**—Subacute bacterial (*Streptococcus viridans*) endocarditis occurs not infrequently as a terminal condition in patients suffering from rheumatic endocarditis with valvular deformity. In a study of 20 cases of endocarditis of the subacute type, H B. Sprague (J. A. M.

A 94 1037 (Apr 5) 1930) found that in all the cases in which the mitral valve was shown to be affected at autopsy (19) a systolic murmur had been noted clinically. In 9 cases a mitral diastolic murmur was heard, but in only 1 instance was it loud and then there was also a loud systolic murmur. In only 2 cases was there an accentuation of the first sound at the apex. Pathologic examination revealed that well-marked constriction of the mitral valve is uncommon in this condition, the circumference of the valve being 8 cm or more in all adolescent and adult hearts of the series (19). Involvement of the aortic valve was present in 11 of the 20 cases. On the basis of these findings, the author believes that when mitral regurgitation persists without the development of mitral stenosis of marked degree, there is greater likelihood of the patient's acquiring subacute bacterial endocarditis than when the valve becomes definitely stenotic within a few years. This conclusion is in accord with the observation of S A Levine (New England J Med 198 885 (June 14) 1928), regarding bacterial endocarditis, *vis*, that "it is those patients who either have aortic insufficiency or who have a mitral systolic murmur without evidence of mitral stenosis who are the most vulnerable in this regard."

**Changes in the Spleen.**—Enlargement of the spleen is quite a constant finding in subacute bacterial endocarditis. H. Fox (Arch Path. 10:402 (Sept) 1930) studied the morbid anatomy of the spleen of 25 cases in which during life or at postmortem examination, or both, *Streptococcus viridans* had been isolated from the blood. According to Fox, the most frequent lesion is the infarct, which is present in 62 per cent of cases. Practically every case

shows perisplenitis, whether or not an infarct is present. In the early stages there is no great enlargement, the organ being merely soft and congested, but in the later stages there is definite enlargement, the result of hyperplasia and the inflammatory changes incident to infarctions. Hyperplasia of lymphatic elements proper is not a feature, but hyperplasia of cells of the reticulo-endothelial series appears in the cases of long duration. Polymorphonuclear neutrophils are prominent, and frequent eosinophils and occasional clasmaticocytes are seen. Marked changes of the linings of the blood vessels are not an outstanding peculiarity of this disease. Evidences of destruction of blood are missing in early, but present in older, cases. Degenerations and coagulation within germ centers are frequently observed. Structures suggesting Bracht-Wachter bodies were seen several times.

**Myocardium in Yellow Fever.**—In electrocardiographic studies during the course of experimental yellow fever in monkeys, W. Lloyd (Am Heart J 6: 483 (Apr.) 1931) found constantly bradycardia, regular in rhythm, absolute in degree, and progressively more marked on succeeding days of the disease. This phenomenon persisted independently of ether anesthesia, sodium iso-amyl-ethyl barbiturate anesthesia, and bilateral section of the vagus nerves. Prolongation of the auriculo-ventricular conduction time was observed in slight or moderate degree in 84 per cent. of cases. In 74 per cent, the T-wave was negative, diphasic or increased in amplitude. Histopathological examination of the myocardium (*Ibid*, p. 504) showed the existence of generalized well-marked degenerative changes of protean character. For the most part, the changes consisted of fatty and gran-

ular types of degeneration. In lesser degree, hyaline and vacuolar types of degeneration were encountered, and occasionally patchy myolysis of isolated muscle fiber groups and small petechial hemorrhages were observed. Only rarely, were cellular infiltrations consisting of small numbers of lymphocytes and endothelial leukocytes found. These degenerative lesions represent a structural basis for the functional disturbances observed.

**PHYSIOLOGY.—Reversal of Flow in the Cardiac Veins.**—O. V. Batson and S. Bellet (Am Heart J. 6: 206 (Dec.) 1930) offer a new explanation as to how the nutrition of the myocardium can be maintained after slow complete occlusion of both coronary arteries. Attention is called to the fact that the myocardial capillary bed has 3 sets of connecting vessels, *viz*, the arteries, the veins, and the sinusoidal vessels (in which are included the Thebesian veins). Other investigators have advanced the hypothesis that in cases surviving double coronary occlusion the capillary bed of the heart receives blood entering the sinusoidal vessels from the heart chambers. Not being satisfied with this theory, these workers performed experiments to ascertain whether blood might reach the capillary bed by way of the coronary sinus and venous system under conditions simulating double coronary artery occlusion. Particles of matter (carborundum or graphite) too large to pass through the lung capillaries were injected intravenously in anesthetized dogs. Any particles, therefore, found in the myocardial circulation would be obliged to come from the right side of the heart through the ostia of either the venous or the sinusoidal circulation. Particles were uniformly found in the

coronary sinus and the coronary veins; and the sinusoidal vessels were excluded as a possible source of these particles in the veins. They concluded that, with a low pressure in the capillary bed (such as attends double coronary occlusion and under the conditions of their experiments), a reversal of blood flow occurs in the coronary veins, the blood then being forced from the capillary bed during the next ventricular systole. A flow and ebb circulation of this character might well maintain proper nutrition of the myocardium in complete double coronary occlusion.

Certain important clinical applications of their work are discussed. It is a well-known fact that the pain of angina pectoris often disappears with the onset of congestive failure, auricular fibrillation or complete heart-block. If the pain is due to an anoxemic state of the myocardium, the anoxemia might be relieved by the reversal of blood flow occasioned by the increased intra-auricular pressure present in congestive failure and auricular fibrillation, and by the long period of ventricular diastole in complete heart-block (during which the coronary artery pressure falls to an extremely low level, and the auricular contractions persist). Also recovery from ventricular fibrillation may be attributed to the reversal of blood flow in the coronary veins, since in this condition it is difficult for proper nourishment of the ventricular muscle to be maintained through the arterial circulation.

**RHEUMATIC HEART DISEASE.—*Diagnosis in Children.***—R. Miller (Brit. M. J. 1.230 (Feb 8) 1930) emphasizes the fact that the early signs and symptoms of rheumatic infection in a child are very various and (for the most part) slight and rather indefinite, and that the best method of

controlling the disease is to diagnose and treat every individual case at the earliest possible moment.

No matter how abrupt the onset of a serious attack of rheumatism may be, almost invariably premonitory symptoms have preceded the attack for weeks or months, but are often overlooked, neglected or misinterpreted. Diagnosis is most easily reached through consideration of the general appearance and deportment of the child (often enough, very characteristic to one familiar with rheumatic children), and by a detailed consideration of the various signs and symptoms—including an examination of the heart. Miller does not believe in the rheumatic diathesis, based on a hereditary tendency. It has been shown that the familial tendency has been exaggerated, being not more than can be accounted for by the frequency of the disease and the environmental causative factor. Nor does he approve of the term "pre-rheumatic child," as such a child is the ordinary rheumatic child with nothing "pre" about it, except that it has not yet suffered a severe acute attack of the infection. In this stage, repeated minor infections keep lowering the child's resistance and so pave the way to a major attack.

The *prodromal stage* is the time before the attack is severe enough to send the child to bed. In this stage there are 4 groups of symptoms:

1 *Constitutional Symptoms*—Juvenile rheumatism is due to a generalized systemic infection, but its slighter, earlier symptoms are mostly due to a general rheumatic toxemia. There results general constitutional ill health, not in itself very specific or diagnostic, but recognizable by its association with rheumatic symptoms. These must be thoroughly studied to avoid mistaking



them for other conditions. The rheumatic child is pale, rather sallow, and unhealthy in appearance, with poor appetite, irritable disposition, and restlessness in sleep. Slight shortness of breath and possibly a dry cough are present, and the temperature and pulse may be elevated in the evening. The only characteristic appearance may be a flushing of the cheeks in a hot room (a typical mauve tinge in the pink flush). This condition may be mistaken for early pulmonary tuberculosis. The diagnosis between the early rheumatic and tuberculous child is not difficult, as a rule, in that the general appearance of the two is different; and in difficult cases the typical rheumatic pains may be the deciding factor.

2. *Throat and Pains Group* — Sore throats are common in rheumatic children, but may be absent when the tonsils are small and buried—a type which may be associated with ultimate mitral stenosis. Signs of tonsillar infection are more important. Septic tonsils are present in 80 to 90 per cent of rheumatic children. Chronic tonsillar sepsis usually presents the following signs: (a) Tonsils seldom very large, and may even be small and buried, (b) tonsillar surface red in the acute phases, and cryptic and irregular in chronic cases, (c) crescentic areas of redness on the faucial pillars where they cover the buried parts of the tonsils, (d) lymphadenopathy at the angles of the jaw, (e) purulent material expressible from the crypts. All these signs are not of equal value.

The characteristic rheumatic pains occur in the vicinity of the joints; are improved with rest and aggravated by exercise, and may be accompanied with slight fever. They may be sharp, or more like a dull aching pain. Not all

muscular pains in children are rheumatic. Pains in the arms, wrists and fingers are usually rheumatic, as is also a stiff neck without lymphadenopathy. In the group of sore throats and pains a certain number of children develop serious rheumatism, usually arthritis and heart disease, with perhaps nodules. The association between tonsillitis and chorea is not so close as that between tonsillitis and arthritis.

3. *Nervous Group* — Rheumatism is a nerve poison. When the brain is affected severely by toxemia or infection, the syndrome of chorea results; but long before this condition appears there is clinical evidence of nervous system involvement. No child with any degree of rheumatism escapes brain affection, some being affected more than others ("latent chorea"). There is general nervous instability, with sleeplessness, sleep-walking, enuresis, tics, etc.

4. *Cardiac Group* — Sometimes the heart is the only diagnostic proof of rheumatic infection. In examining the heart it is important that the examination be made in the supine as well as in the erect position, and also with the child lying on the left side. The following are signs of cardiac involvement in early juvenile rheumatism: (1) Increased pulse rate—which is of no diagnostic value unless accompanied by (2) dilatation of the ventricle (myocarditis). (3) An apical systolic murmur, audible in any of the positions mentioned (and clearly not a cardiorespiratory bruit), accompanied by left ventricular enlargement, renders the diagnosis of rheumatism practically certain. (4) The presence of a reduplicated apical second sound, or of a mid-diastolic apical murmur, is also strong evidence of rheumatism. (See Early Diastolic Snap of Mitral Stenosis under

Heart Sounds )—ED Certain cases present persistent tachycardia.

*Prevention* of early juvenile rheumatism can be accomplished by the removal of focal infections, improving the environment, and protecting the child against the exciting causes of acute attacks.

C F Coombs (Brit M. J. 1 227 (Feb. 8) 1930) believes that a child becomes rheumatic because defects of inheritance and of environment combine to subject him to invasion by organisms that the healthy child can resist. In a third of all the cases the portal of entry is the tonsils. Two-thirds of the rheumatic children are first infected between the ages of 5 and 15 years, a large proportion being drawn from the elementary school population. The principal tissues affected are the heart, joints, meninges, and subcutaneous tissues. There is undeniable proof that a child whose general condition is fair, with normal temperature and cardiac signs unaltered, may nevertheless be found, after a period of apparently uneventful weeks, to have grown worse, and the heart at postmortem examination may show definite proof of infection which must have been active for weeks before death. This is evidence of the persistence of the infection, in contrast to the view that the disease shows periods of activity, separated by intervals of quiescence. The heart lesions are distributed in the myocardium, endocardium and pericardium.

Early recognition of rheumatic heart disease can be accomplished only by bearing in mind the possibility of other rheumatic phenomena occurring long before symptoms of cardiac insufficiency appear. There are 4 different approaches to a diagnosis of cardiac rheumatism in the early stages:

1 The presence of *arthritis pains* or *chorea*. Pain persisting more than a day, or one that causes lameness (particularly if the child looks ill or has a fever) should be given proper attention. Every child with recognized rheumatic polyarthritis may be assumed to have an infected heart also, even though symptoms and signs of such involvement are lacking. Many children recover from an attack of chorea without showing signs of cardiac infection, but many show such signs later.

2 *Tonsillitis*.—Repeated examination of the heart should always be made in a patient with tonsillitis. Signs of cardiac involvement may not appear until some time after the attack, therefore, convalescent children should be examined a few days after obvious symptoms have cleared up.

3 Definite (and permanent) *damage of the heart* may occur without any other perceptible sign of rheumatic infection. In a large group of children the cardiac lesion is not discovered until the chest is examined for some other illness or during routine inspection in the school medical service. The earliest symptoms of the so-called latent cases are purely constitutional, *i.e.*, loss of appetite, vague seediness, increasing pallor, and (above all) loss of weight.

4 A few cases show *cardiac symptoms in the beginning*. There are 2 groups: (a) those becoming acutely ill, with fever and chest symptoms, when the first impression may be pneumonia or pleurisy, and only after a few days may a pericardial friction rub or a rapid widening of the area of cardiac dullness indicate heart trouble; (b) those showing breathlessness.

In making the diagnosis of carditis, arrhythmia in a child means nothing unless it is supplemented by evidence of

serious organic heart disease. Exaggeration of the physiological sinus arrhythmia is insignificant, particularly during convalescence from acute illness. The total arrhythmia of auricular fibrillation is very rarely seen in children with rheumatic carditis. With the exception of the diastolic murmur of aortic incompetence (which may be the only sign of carditis in a rheumatic child), a murmur alone is not evidence of cardiac disease in childhood. The earliest phase of cardiac rheumatism that can be diagnosed with certainty is characterized by the coincidence of 4 physical signs: (a) Increased area of cardiac impulse to the left; (b) accentuation of the first sound at the apex; (c) a systolic murmur, limited to or maximal at the apex, and (d) an accentuated pulmonic sound. Even without a rheumatic history and the absence of any symptoms, these signs indicate cardiac rheumatism in a child.

A systolic murmur, audible only at the apex, without other signs, justifies a waiting attitude. If the murmur is general all over the heart, it should be regarded with suspicion if it arises after an attack of tonsillitis or chorea. Generally, the younger the child, the more likely are these signs to prove evanescent. In a child of 10 years or older, the certainty is greater; however, a child should not be kept in bed because of the murmurs alone. Many organic murmurs at the apex are inaudible when the patient stands, but are brought out clearly when lying down, and especially when lying on the left side.

An increased area of impulse alone, even without alteration in the sounds, is to be treated with respect. If the child is suspected of having had a recent active infection, it should be kept in bed, or on restricted exercise, until the active

infection is ended. If there is a history of previous though extinct rheumatic infection, the child should be re-examined repeatedly for 12 months at least. These precautions are especially indicated if the heart sounds are changed.

**Treatment.**—Complete rest in bed is indicated whenever there is any symptom of active infection, such as fever, wasting, joint pains, or chorea—at all events at first, in order to overcome the infection, and to allow the physician to assess the degree of activity and to determine the treatment. The symptoms requiring prolonged rest are continued pallor and wasting, fever, nodes, chorea, recurring joint pains, and progress in the definition of the physical signs. Supervised exercises are helpful during convalescence. During quiescence, restrictions are unnecessary, and may even be harmful.

Fever is not an infallible guide to treatment. Two types of fever are seen in rheumatic infection. Sometimes an otherwise normal temperature is disturbed by periods of pyrexia varying from 2 to 3 days to as many weeks. Such outbursts of infection are rarely overlooked. The other type is more insidious, showing daily fluctuations above the normal, and persisting for weeks. An absence of fever does not prove the absence of infection. Some of the worst cases are afebrile, possibly owing to poor resistance. In such cases there is usually abundant evidence of disease, such as pallor and loss of weight, stationary or ingravescent cardiac signs, and hints of circulatory failure, such as faint cyanosis, enlargement of the liver, edema, etc. Nor is the leukocyte count a reliable guide to treatment. There is no rule as to duration of rest in bed. Any febrile event lasting more than 4 days indicates rest for at least 4 weeks.

Return to activity must be gradual, being conditioned by the happenings during the rest period and also by the response to exercise.

Coombs (*loc cit*) believes that it is practically always safe to give salicylates in big doses, occasionally untoward symptoms may develop, and then the drug must be stopped. If the drug is not doing any good, the dose may be too small, or another preparation—like aspirin—should be tried.

Periods of rest, combined with fresh air, sunlight and a liberal diet with plenty of fats, usually proves of benefit. Cod-liver oil and iron may be given, even when taking salicylates. Tonsillectomy is considered by many as a routine measure. Coombs has the tonsils removed if they are obviously diseased—with an associated adenitis, or if they are enlarged. He believes that an acute inflammatory process in the tonsil should be allowed to recede before the tonsil is removed, to avoid recrudescence of the infection.

See also article on Heart Diseases in Children.

**HEART SOUNDS.—“Extra” Heart Sounds.**—Interest in the so-called “extra” heart sounds should be stimulated by reading the article of C C Wolferth and A Margolies (M Clin. North America 14 897 (Jan) 1931), in which they state that the clinical differentiation among the various types of these sounds is not difficult if the clinician looks for these features during each cardiac auscultation. The main points in the differential diagnosis of the various “extra” sounds are presented in the table on following page.

A *reduplicated* or *split first heart sound* can be the result of at least 2 mechanisms. In bundle-branch block and in ventricular extrasystoles it is pos-

sible that the doubling is caused by asynchronism in the beginning of contraction of the 2 ventricles. This view is supported by the fact that in these cases the second sound also is usually split, suggesting that dynamic systole in one ventricle is completed before that of the other. The reduplication which occurs in healthy individuals with a normal electrocardiogram presumably results from a slight delay in the closure of the auriculoventricular valves. Reduplication of the first sound is frequently so closely simulated by presystolic gallop rhythm that it may be impossible to differentiate them by auscultation.

The authors point out that there are but 2 fundamental types of *gallop rhythm*, *vis*, presystolic and protodiastolic. *Presystolic* gallop is always associated with auricular contraction, usually beginning 0.12 to 0.16 second after the upstroke of the P-wave. The “extra” sound of *protodiastolic* gallop has many points of similarity to the third heart sound, occurring in a range approximately 0.12 to 0.20 second after the second sound. The authors also describe a *summation form* of gallop—a combination of presystolic and protodiastolic gallop—which they classify as the most important of all from the clinical point of view. The gallop sound usually occurs from 0.12 to 0.20 second after the second sound and shortly before the next first sound. It is found chiefly in patients with severe *hypertensive cardiovascular disease* and *tachycardia*. In that the gallop sound may be as loud or even louder than the first or second sound, it is overlooked much less frequently than the other types of gallop. The presence of either tachycardia or a prolonged auriculoventricular conduction time is believed necessary

TABLE I  
SOME OF THE DIFFERENTIAL POINTS WHICH MAY BE FOUND OF VALUE IN THE DIAGNOSIS OF "EXTRA SOUNDS"

	Point of Maximum Intensity	Usual Time Relation	Character	Remarks
Reduplicated first sound	Apex or just to left of lower part of sternum	Interval 0.06-0.12 sec	Both sounds similar or second sharper and higher pitched	Easily differentiated by the time relation from all extra sounds except late presystolic gallop. If the latter sound is sharp, clinical differentiation may be impossible.
Reduplicated second sound	Base	Interval 0.03-0.11 sec	Both sounds usually have similar character	The only extra sound with point of maximum intensity at the base.
"Physiologic" third heart sound	Inside apex, usually fourth interspace	0.12-0.18 sec after second sound	Faint, short low-pitched	Cannot be distinguished from protodiastolic gallop except by absence of heart disease.
Protodiastolic gallop	Inside apex, usually fourth or fifth interspace	0.12-0.20 sec after second sound	Faint, low-pitched, may be short murmur	Point of maximum intensity, time relation to second sound, and character all important. Cannot be distinguished from physiologic third sound except by the presence of heart disease.
Presystolic gallop	Inside apex, usually fourth or fifth interspace	0.14-0.04 sec before first sound	Faint, low-pitched, may be short murmur	Ability to time it before the first sound is most important.
Summation form of gallop	Inside apex, usually fourth or fifth interspace. May be just to left of sternum	Mid-diastole, usually 0.12-0.18 sec after second sound	Low-pitched, may be faint, loud, or short murmur	The most important clinical form. The rate always exceeds 100 beats per minute unless delayed conduction is present. Occurs when auricular systole falls close to the preceding ventricular beat.
The early diastolic snap	Just below mitral ring. Third or fourth interspace	0.07-0.13 sec after second sound	Sharp snap or clicking sound	The point of maximum intensity, the time and character of the sound differentiate it from all other extra sounds.
Midsystolic click	Inside apex, fourth or fifth interspace	Approximately midway between first and second sounds	Sharp snap or clicking sound	The position in the heart cycle differentiates it from all other extra heart sounds.

for the production of a loud gallop sound, which represents the summation of 2 factors, *viz*, the inrush of blood in early diastole and auricular systole occurring synchronously

**Early Diastolic Snap (Claquement d'Ouverture de la Mitrale).**—A. Margolies and C C Wolferth (Tr. Am Clin. and Clin Ass 46 87, 1930) recall to attention the early diastolic snap (*claquement d'ouverture de la mitrale*) of *mitral stenosis*, clearly described by Duroziez in 1862. This sound can be heard in over half the cases of mitral stenosis, whether or not a mitral regurgitant murmur is present. It is not infrequently confused with reduplication of the second sound at the base. Usually it is heard best slightly below the anatomic position of the mitral valve as a sharp snap or click, occurring 0.07 to 0.13 second after the beginning of the diastolic murmur, although the points of maximum intensity of the two are not the same. The murmur is heard best lower and to the left (nearer the apex). The snap is heard in the presence of auricular fibrillation almost, if not quite, as distinctly as in the presence of regular sinus rhythm. In auricular fibrillation variations occur in the time relation of the early diastolic snap to the second sound, the intervals after premature beats being shorter. These changes are readily explained on the assumption that the sound is due to the opening snap of a stenosed mitral valve. In the differential diagnosis of this sound, the so-called third heart sound, reduplication of the second sound at the base, gallop rhythm, and clicking sounds occurring sometimes about the middle of ventricular systole must be considered. The chief diagnostic value of the sound is to call attention to the possibility of mitral

stenosis. By far *the most valuable clinical sign of mitral stenosis is the characteristic diastolic murmur*, however, in the absence of the murmur, with a history of rheumatic fever, a sharp first sound at the apex, and enlargement of the left auricle, the early diastolic snap is additional cumulative evidence of the presence of mitral stenosis.

**Auricular Contraction and the First Heart Sound**—C C Wolferth and A Margolies (Arch Int Med 46 1048 (Dec) 1930) have studied the influence of auricular contraction on the first heart sound and the radial pulse. Striking variations in the intensity of the first heart sound in complete *heart-block* were described by T W. Griffith (Heart 3 143 (Feb) 1912), who found the loud beats to occur when the contractions of the auricles and ventricles were almost synchronous. T Lewis ("Lectures on the Heart," Paul B Hoeber, Inc, New York, 1915) pointed out that the inequalities of sound in complete heart-block are pronounced, and that the variation in sound is a valuable bedside test of *auriculoventricular dissociation*.

In a study of a series of 7 cases with varying auriculoventricular relationships, Wolferth and Margolies found all to show inequalities of the first heart sound which were related to the lengths of the intervals between the auricular and ventricular systoles, but the louder first sounds did not always occur when the auricular and ventricular contractions were practically synchronous. In addition, by taking simultaneous heart sound and pulse wave tracings, they found that either comparatively loud or faint sounds may be associated with comparatively large or small pulse waves. In conclusion, they present the hypothesis that irregularities of the first



heart sound result principally from variation in the position of the mitral leaflets at the beginning of ventricular contraction, and that the changes in the amplitude of the pulse waves are chiefly due to the effects of auricular systole on ventricular filling and initial tension

**CARDIOVASCULAR SYPHILIS.**—At the 1930 annual meeting of the American Heart Association there was held a symposium on Cardiovascular Syphilis, which represented the first results of the efforts of that Association to encourage coordinated research in the various phases of cardiovascular disease.

**Pathology.**—From a clinical and pathological standpoint, H S Martland (Am Heart J. 6 1 (Oct) 1930) believes that syphilis of the aorta and heart should be regarded as an acquired disease (congenital cases being infrequent), developing insidiously and showing symptoms years after the initial infection. Acquired cardiac syphilis, he states, is essentially a supravascular sclerosis which may manifest itself in one or more of the following ways: (1) Small isolated patches of sclerosis in locations doing little damage; (2) larger areas of sclerosis which become confluent, converting the aortic arch into a thick rubber tube; (3) triangular patches of sclerosis which infiltrate between the commissures of the aortic cusps causing regurgitation; (4) extension of the scarring process over the coronary ostia with narrowing or complete atresia of one or both arteries; (5) weakening of the aortic wall and production of an aneurism, which is especially liable to occur when the aortic valve remains competent. In his mind, syphilis involving other parts of the heart is unusual, and is of no great clinical or pathological importance.

Specific lesions of the myocardium are infrequent, and, when they occur, are so slight as to be of little practical importance. When the aortic valve is involved, the main myocardial lesion is hypertrophy.

In a study of 119 cases in which the diagnosis of syphilitic aortitis was made at autopsy, J G Carr (Am Heart J 6 30 (Oct) 1930) found that, except for the predominant left ventricular hypertrophy which resembles that of essential hypertension, the gross myocardial changes associated with syphilitic aortitis are not characteristic. Fifty-one of the hearts weighed over 450 grams, 44 between 300 and 450 grams, and 19 less than 300 grams. Aortic insufficiency was found in about 20 per cent. of the specimens, occurring most frequently in the advanced cases, it was present in 19 (37.2 per cent) of the hearts weighing over 450 grams. Aortic aneurism was found in 13 cases, occurring more frequently in the cases characterized by relatively minor cardiac symptoms. Carr believes that hypertrophy of the heart is a significant index of the degree of cardiac involvement in cardiovascular syphilis, and that it is the result of aortic regurgitation and hypertension (which latter is a common finding in this type of case).

O. Saphir and R W Scott (Am Heart J 6 56 (Oct) 1930) studied the pathological features of 107 cases of syphilitic aortitis with involvement of the aortic valve area. Characteristic gross syphilitic lesions were found at the aortic root in all cases, extending upward as far as the arch of the aorta in all but 2 instances. In 20 cases gross lesions were present in the descending aorta. Aneurismal dilatation of the aorta was found in 16 instances. The authors express the opinion that the pri-

mary and earliest lesion in syphilis of the aorta and the larger vessels is an obliterative endarteritis of the vasa vasorum of the adventitia, with perivascular infiltration of lymphocytes. The medial changes are thought to be secondary, being attributable to nutritional disturbances. All cases showed some degree of deformity in the architecture of the aortic cusps, the commonest finding being a widening of the commissure. The syphilitic process spreads from the aorta to the aortic valves by way of the small vessels at the commissure. In 82 instances the commissures were the seat of hyaline plaques. Thirty-seven cases (33 per cent) showed some constriction of the mouths of the coronary arteries. Four cases showed complete obliteration of the left coronary orifice, and in 1 there was complete obliteration of the right. In no case was there any evidence of syphilis in the coronary arteries beyond the orifices. No characteristic gross lesions of syphilis were present in any of the larger arteries (carotid, subclavian, innominate, mesenteric, iliac, and femoral), however, quite a few microscopic lesions were observed. In no instance was there found gross or histological evidence to warrant syphilitic involvement of the myocardium. The changes in the myocardium differed in no way from those occurring in hearts hypertrophic from other causes, or in hearts the seat of coronary sclerosis. *Spirochæta pallida* were not found in spite of repeated studies.

C. C. Maher (Am Heart J. 6.37 (Oct) 1930) studied microscopically sections from 5 cases of uncomplicated and probably untreated aortic regurgitation. The main coronary arteries and their branches were found to be the seat of a lymphocytic and plasma cell infiltration (exactly like that seen in the

aorta), not infrequently exceedingly dense in the first few centimeters of their courses. The invasion is characteristically located in the adventitial coat but may invade the media of the subintima. Localized groups of lymphocytes were commonly encountered in the visceral pericardium and beneath it, though a more common finding was a more scattered infiltration of these same cells. In the myocardium, localized areas of infiltration were found between the fibers and about the capillary walls.

From the pathological findings observed in 3 cases, J. W. McMeans (Am Heart J. 6.42 (Oct) 1930) expresses the belief that in syphilitic aortitis the intima is involved from the adventitia through the vasa vasorum. (The lesions are the same histologically.) He calls attention to the fact that intimal lesions due to syphilis are well recognized in small vessels under the term endarteritis proliferans, and, therefore, luetic intimal disease is not a peculiar condition. In his mind, aortic regurgitation, and also closure of the coronary orifices, associated with syphilitic aortitis, can only be produced by involvement of the aortic intima, the media not entering the picture at all.

**Heart Findings in Congenital Syphilis.**—In a study of 50 cases of congenital syphilis, under active treatment, G. Previtali, G. H. B. Nicolson and D. Moon-Adams (Am. Heart J. 6.128 (Oct) 1930), in spite of a most painstaking search, were not able to find evidence of any cardiovascular lesion. Physical examinations and teleoroentgenograms were negative. In no case was the aortic arch widened. Electrocardiograms showed normal rhythm with no delay in conduction, no abnormalities of deflection, but frequent low voltage. Children of varying age groups

presented no differentiation in physical signs

Four hundred and seventeen cases of congenital syphilis, ranging in age from 3 months to 42 years, were studied by T B Givan (Am Heart J 6 132 (Oct) 1930), and in not one were there signs warranting a definite diagnosis of syphilis. In no case did autopsy reveal sufficient changes in the heart to account for death, although interstitial myocarditis, vacuolization of the muscle fibers and the *Spirocheta pallida* were demonstrated. Usually a terminal pneumonia, and occasionally a syphilitic meningitis, accounted for death.

H McCulloch (Am Heart J 6 136 (Oct) 1930) reports the finding of 939 cases (23 per cent) with congenital syphilitic infection among 40,470 children under 15 years of age, admitted to the out-patient department of the St Louis Children's Hospital during a 10-year period. Of the children with syphilis, 441 were under 2 years of age. Evidence of syphilitic heart disease was found in 3 of 32 autopsies of infants under 2 years of age. None of the children living up to the age of 15 years has died suddenly or shown signs of heart disease similar to syphilitic heart disease seen in adult or later life.

**Clinical Course of Aortic Insufficiency.**—In a study of 107 autopsied cases of syphilitic aortic insufficiency (individuals from the working class, the majority negroes), R W Scott (Am Heart J 6 86 (Oct) 1930) found that syphilitic involvement of the aortic orifice may appear as early as 5 years and as late as 48 years after the primary infection (the average time interval being about 20 years). The youngest patient was 23 years old and the oldest 79 years. Fifty-nine of the

patients died between the ages of 40 and 60 years, 25 between 30 and 40 years: 5 between 20 and 30 years, 15 between 60 and 70 years, and 3 between 70 and 80 years. Free aortic regurgitation appearing out of a clear sky in an adult with a negative cardiac history and with no evidence of infection should be regarded as syphilis until proved to the contrary. The more or less abrupt appearance of cardiac symptoms, and the progressive nature of the heart failure characterized the clinical picture. The first subjective symptoms in the majority of cases were those of beginning heart failure, *viz*, dyspnea on exertion, palpitation and edema of the lower extremities. Precordial and substernal pain, or anginal attacks, were seldom noted except in those cases with marked narrowing of the coronary arteries, however, even with marked constriction of the coronary orifices, chest pain was not always present. In 99 cases varying degrees of congestive failure were present at the time of death. The cardiac mechanism remained normal in all but 5 cases, 3 of which had auricular fibrillation and 2 paroxysmal auricular tachycardia. The appearance of congestive failure in syphilitic aortic insufficiency is a grave omen.

**X-ray Diagnosis.**—C M Kurtz and J A E Eyster (Am Heart J 6 67 (Oct) 1930) report the finding of fluoroscopic evidence of aortitis in 90.7 per cent of 54 cases of acquired syphilis, and in 36.4 per cent of 12 cases of congenital syphilis. The diagnosis was based upon the following points: (1) The shape of the ascending aorta; (2) the presence of pulsation to the right of the sternum, and (3) the density of the descending aorta. Aneurism of the aorta was found in 18.5 per cent. of the cases of acquired syphilis, and in none

of the congenital cases. Of special interest was the demonstration of aortitis in 22 (95.7 per cent) of 23 patients suffering primarily from syphilis of the central nervous system (the average duration of which was 20 years).

In an analysis of the x-ray findings in 40 cases of syphilitic aortitis, proved by autopsy, D. Steel (Am. Heart J. 6: 59 (Oct.) 1930) states that the following points are present in well-marked cases: (1) A dense aortic shadow often with hazy borders, (2) a high, dense and prominent aortic knob; (3) irregular and also general dilatation; (4) increased pulsation, (5) association with aortic insufficiency. He believes that the increased density is largely due to the increased diameter of the blood column incident to dilatation, and possibly partly to changes in the wall. In his mind, the most important sign is irregular dilatation—appearing as one or more localized spindle-shaped areas, not aneurismal in dimension—involving most commonly the root. In the later stages, dilatation may become diffuse.

R. Ingraham and E. P. Maynard, Jr. (Am. Heart J. 6: 82 (Oct.) 1930) were not able to demonstrate any definite electrocardiographic or teleoroentgenographic evidence of disease of the heart or aorta in 27 cases of early syphilis (a year or less in duration).

**Relation of Syphilis to Hypertension.**—Because of conflicting statements as to the incidence of syphilis in hypertension, E. F. Horine and M. M. Weiss (Am. Heart J. 6: 121 (Oct.) 1930) studied a group of 666 patients with essential hypertension to determine if syphilis were a possible etiological factor. The incidence of syphilis in the hypertensive group was found to be practically the same as in a control group of 2000 nonhypertensive patients

of similar ages and economic status. They conclude, therefore, that syphilis has no etiological bearing on essential hypertension.

**Treatment.**—The treatment of cardiovascular syphilis differs with the individual status of every patient. J. E. Moore and J. H. Danglade (Am. Heart J. 6: 148 (Oct.) 1930) advise that if *heart failure* is present, the patient should be treated with routine medical measures, such as rest, restriction of activities and digitalis, until compensation is regained; and then antisyphilitic treatment should be begun cautiously. Both the danger of therapeutic shock (Herxheimer reaction) and of precipitating decompensation by the too rapid resolution of syphilitic inflammatory tissue weigh against the initial use of the arsphenamine products. Treatment with bismuth or mercury and potassium iodide is instituted for at least 10 or 12 weeks; and then, if the patient's cardiac reserve seems adequate, a course of 10 to 12 weekly injections of small doses of neoarsphenamine or bismarsen (bismuth arsphenamine sulphionate) are administered. Treatment is kept up for a minimum period of 2 years, and often indefinitely, courses of neoarsphenamine alternating with courses of bismuth and the iodides. Moore and Danglade found that the life of patients with aortic insufficiency may be prolonged from an average of 32 months from the onset of symptoms in untreated patients to an average of 65 months in patients receiving 1 year or more of such treatment.

L. E. Hines and J. G. Carr (Am. Heart J. 6: 142 (Oct.) 1930) report symptomatic improvement in 57 per cent of 88 cases of cardiovascular syphilis treated with neoarsphenamine. A higher percentage of improvement was

noted in patients with syphilitic aortitis without definite aneurism or aortic regurgitation. In 12 per cent of the patients the symptoms were aggravated. In 3 instances probably anatomical damage was occasioned, *i e*, kidney damage in one, increase in signs of aortic insufficiency in another, and in the third, acute red atrophy of the liver or aneurismal rupture were observed. Improvement in the serological reactions of the blood did not always parallel the symptomatic improvement. It was concluded that patients functionally classed 2B (American Heart Association) may be benefited by neoarsphenamine if cautiously administered in small doses.

U J Wile (Am Heart J 6 157 (Oct) 1930) believes that, with the exception of tryparsamide in certain selected cases of *aortitis*, better results are obtained by the conservative use of mercury, bismuth and iodides than by the arsphenamines.

[The results of these studies show that the treatment of cardiovascular syphilis is not a hopeless procedure.—Ed]

#### THYROID AND HEART DISEASE.—*Size of Heart in Goiter.*—

The influence of goiter on the size of the heart remains an unsettled question. In a series of patients studied by H. Meyer-Borstel (Fortschr a d Geb d Rontgenstrahlen 41 695 (May) 1930), 83 per cent of those with toxic goiter and 59 per cent of those with simple goiter presented cardiac enlargement. He concludes that most goiter patients have cardiac enlargement. The enlargement may be generalized, but he believes the typical form involves chiefly the right ventricle.

In a teleoroentgenographic study of 100 consecutive cases of nontoxic goiter in the Lahey Clinic, L. M. Hurxthal,

O J Menard and M E Bogan (Am J M Sc 180 772 (Dec) 1930) could find no definite relationship between the duration of the disease or weight loss and the size of the heart. Even in long-standing hyperthyroidism of high degree in younger people the heart was often of normal size. Cardiac enlargement, however, did show a fairly direct relationship to age and coincident cardiovascular disease. In that the number of enlarged hearts of different degrees was practically the same in both the toxic and the nontoxic groups, it was concluded that, if hyperthyroidism causes cardiac enlargement (hypertrophy or dilatation, or both), it does so only to a slight degree.

H M. Thomas, Jr (Bull Johns Hopkins Hosp 47.1 (July) 1930) reports 2 quite similar cases of exophthalmic goiter with severe myocardial insufficiency, 1 of whom died after subtotal thyroidectomy, while the other achieved complete clinical recovery. The latter case demonstrated the fact that even the most severe intoxication from hyperthyroidism need not produce permanent functional cardiac damage. In the first case, even though death resulted from heart failure, there was no pathological evidence of significant myocardial damage. Thomas states that descriptions of the anatomical changes found in patients dying of thyroid heart disease are universally lacking in evidence of permanent heart damage. Changes that have been described in the literature are: (a) Marked cardiac dilatation, usually most pronounced on the right side; (b) slight cardiac hypertrophy, (c) variable, slight degree of scattered perivascular round cell infiltration; (d) hyaline and fatty degeneration of the muscle fibers. Many investigators agree with the conclusion of F A. Willius, W M. Boothby

and L B Wilson (M Clin North America 7 189 (July) 1923). "At necropsy insufficient evidence is disclosed to ascribe death to cardiac causes. Although in most cases degenerative changes were found, they could not be considered the dominant factor producing death. The finding of fatty degeneration of the heart, which in some cases is no more than that found in persons who die of old age, appears to be an expression of the effect of a long-continued or intense toxemia, combined with increased activity." F H Lahey (Ann Surg 90 750 (Oct) 1929) also feels that the effect of thyroxin on the heart is temporary and that no changes are produced which may not disappear when the hyperthyroidism subsides. Thomas concludes that, with the evidence at hand, the burden of proof rests on those who claim that permanent myocardial damage results from hyperthyroidism.

D McEachern and G Rake (Bull Johns Hopkins Hosp 48 273 (May) 1931) have studied the morbid anatomy of the hearts of 27 cases of hyperthyroidism and have compared the findings with a series of 150 control cases. Fourteen of the 27 hearts showed no changes of the kind or degree not to be found in the control groups of similar age or which are not well recognized as occurring in general autopsy material in the absence of specific heart disease. Moderate perivascular or intermuscular fibrosis or small round cell infiltration was found in 8 instances; however, similar changes were also encountered among the controls, though less frequently. Five cases presented conspicuous alterations, in 3 of which there was coexistent heart disease. Cardiac hypertrophy was present in 16 of the 27 cases. Congestive failure occurred in 5

of the 6 cases in which there was co-existent organic heart disease. No relationship could be found between the coexistence of auricular fibrillation or the duration of hyperthyroidism and the ultimate findings in the heart. These workers believe that it is impossible to ascribe the cardiac phenomena in hyperthyroidism to structural changes in the muscle. Study of the problem from the viewpoint of metabolic and functional changes in the myocardium is suggested.

In experiments on healthy dogs, J P Simonds and W W Brandes (Arch Int Med 45 503 (Apr) 1930) produced actual hypertrophy of the heart by feeding 10 Gm (2½ drams) of desiccated thyroid daily. The hypertrophy was found to be related to the loss of body weight, occurring in those animals that had lost from approximately 25 to 35 per cent of their original body weight. When the loss of weight exceeded approximately 35 per cent, the heart lost the weight it had gained in hypertrophy, and the final heart weight/body weight ratio approached that seen in simple inanition. The hypertrophy involved all the chambers of the heart with a slightly greater proportional increase in the left ventricle.

**Masked Hyperthyroidism.**—From time to time numerous writers have called attention to the existence of atypical, obscure or masked forms of hyperthyroidism. W W Hamburger and M W Lev (J A. M. A 94 2050 (June 28) 1930) report in detail a group of middle-aged, apathetic men and women patients, suffering with thyrotoxicosis, in whom the classic signs and symptoms of hyperthyroidism were lacking, but who presented an atypical clinical picture of some other type of disease, such as organic heart disease,



congestive heart failure, angina pectoris, diabetes mellitus or pernicious vomiting. The majority of the patients were of the poor class, "burdened with countless worries, apathetic, listless, with masked faces, dulled eyes, quiet and insensitive—in striking contrast to the alert, restless, nervous, bright, prominent eyed patient with hyperthyroidism." A suggestive increased warmth, redness or pigmentation of the skin, slight staring expression of the eyes, increased restlessness, unexplainable loss of weight; and a persistent increase in the basal metabolism suggested the correct diagnosis in these cases; and the final diagnosis of hyperthyroidism was established on the basis of the reaction to compound solution of iodine, thyroidectomy, or the appearance of the gland histologically.

**Heart in Myxedema.**—In an analysis of the 18 hospital cases of myxedema with an average basal metabolic rate on admission of minus 33 per cent by C. L. Tung (*Am Heart J* 7 734 (Aug) 1931), 7 showed evidence of cardiac insufficiency, 9 enlargement of the heart, 7 hypertension, and 7 a definite generalized arteriosclerosis. No definite relation was found to exist between the presence of hypertension or arteriosclerosis and the duration of the myxedematous state. Symptoms and signs of cardiac weakness disappeared under thyroid medication. The electrocardiogram in all cases showed P-waves and QRS complexes of relatively small amplitude. The most striking abnormality was the flattening or inversion of the T-wave. It is of considerable interest to note that this abnormality disappeared after treatment in the 7 cases in which electrocardiographic examination was repeated after the return of the basal metabolic rate to normal.

**Velocity of Blood Flow in Hyperthyroidism and Myxedema.**—The velocity of blood flow in hyperthyroidism and myxedema has been studied by H. L. Blumgart, S. L. Gargill and D. R. Gilligan (*J Clin Investigation* 9: 69-91 (Aug) 1930). The radium active deposit method of determination was used. The velocity in hyperthyroidism was found to be the fastest that has been recorded in man. The increase in velocity was directly proportional to the elevation of the basal metabolic rate. When the basal metabolic rate was lowered by the administration of compound solution of iodine or by operation, the velocity of blood flow was correspondingly reduced. A general but inexact relation was found between the degree of elevation of the pulse rate and the increase in the basal metabolic rate. In 9 patients with thyrotoxicosis but without circulatory failure, in whom the basal metabolism averaged 33 per cent above normal, the velocity of blood flow through the lungs averaged 83 per cent above normal. In 4 thyrotoxic patients with similar basal metabolic rates but slightly slower blood flow, dyspnea developed on slight exertion. The fact that the latter group of patients experienced dyspnea on slight exertion emphasizes the close interdependence of the circulatory-respiratory-metabolic mechanism. In 7 patients with myxedema the blood flow was strikingly slow, corresponding closely to the degree of lowering of the basal metabolic rate. With the administration of thyroid gland substance there occurred a rise in basal metabolic rate and a simultaneous increase in velocity of blood flow, closely paralleling each other. On comparing the changes in the pulse rate, basal metabolic rate and velocity of blood flow in myxedema with those in

thyrotoxicosis, the authors conclude that the increased blood velocity in thyrotoxicosis is due to the increased basal metabolic rate rather than to a specific toxic effect on the heart

### ***Auricular Fibrillation and Goiter.***

—*Treatment with Quinidine*—L M Hurxthal (Am J M Sc 179 507 (Apr) 1930) found quinidine to be the most effective drug in the treatment of postoperative *paroxysmal auricular fibrillation* in a series of 59 thyroid patients. This type of arrhythmia occurs frequently following removal of non-toxic goiters, but more often after partial or subtotal thyroidectomy in patients with primary hyperthyroidism. It is frequently disturbing to the patient, but rarely does it produce any alarming systemic reaction. Often it can be stopped by the administration of digitalis in 12 to 18 grain (0.7 to 1.1 Gm.) doses. In 10 of 15 patients who were given digitalis as soon as possible after the onset, fibrillation ceased within 24 hours after the administration of the drug. Quinidine proved successful in all cases of this type.

About 10 per cent. of patients with hyperthyroidism have *established auricular fibrillation*. This type of irregularity is presented by over 90 per cent of hyperthyroid patients with associated congestive heart failure, and, conversely, from 30 to 40 per cent of those having auricular fibrillation have a history or show various degrees of this type of heart failure. The possibility of embolism must be considered when selecting these patients for quinidine therapy. The *contraindications for quinidine therapy* are as follows: (1) A history of clinical evidence of embolism; (2) marked mitral stenosis with fibrillation of unknown duration; (3) mitral stenosis with congestive heart failure; (4)

congestive heart failure associated with large feebly pulsating heart as determined by fluoroscopy; (5) long-standing fibrillation in hyperthyroid patients in which the hyperthyroidism is of mild degree.

Of 55 cases of established fibrillation, 8 were not given quinidine, 7 stopped spontaneously; in 5 other cases quinidine was not successful; and 34 cases were successfully treated. Intolerance for the drug was seemingly not the cause of failure in its administration, since often smaller doses produced toxic symptoms in those who were successfully treated than in those who were not. Coincident heart disease was the biggest factor in the cause of failure. Recurrence of fibrillation, which occurred in 4 cases, appeared usually due either to recurrence of thyroid toxicity or to coincident cardiovascular disease. The chief *toxic reactions* were nausea (21 cases); "fullness of head" (3 cases); diarrhea (2 cases); and a diffuse punctate skin eruption (1 case).

The *method of dosage* was as follows: Quinidine sulphate, 3 grains (0.2 Gm.), was prescribed after breakfast. If no reaction or unpleasant symptoms developed, 6 grains (0.4 Gm.) were given with  $\frac{1}{2}$  glass or more of fluid every 2 hours until the pulse became regular, unpleasant symptoms arose, or not more than a total of 39 grains (2.5 Gm.) had been given. Because of the rapid absorption of the drug, it was not found necessary to wait longer than 2 hours for manifestations of idiosyncrasy. When this plan of treatment was ineffectual, or when toxic symptoms occurred before heart action became regular, 6 or 9 grains (0.4 to 0.6 Gm.) of the drug were given after each meal for several days. Such dosage may be tolerated by the patient and, if continued,

may prove successful. If success did not attend this procedure, the patient was discharged with a dosage of 3 grains (0.2 Gm.) after meals until his return. When difficulty in establishing normal rhythm was experienced, a daily dose of 6 grains (0.4 Gm.) was continued for 1 or 2 months, to insure permanency of the result.

The author concludes that quinidine is the ideal drug for restoration of normal rhythm from established auricular fibrillation in selected cases of hyperthyroidism.

#### GENERAL TREATMENT.—

##### *Digitalis.—Hepatic Vein Constriction.*

—W. Dock and M. L. Tainter (J. Clin. Investigation 8:467 (Apr.) 1930; *ibid* 485 (June) 1930) call attention to the fact that peripheral resistance and venous return are factors of importance in the governing of the systolic output attending therapeutic doses of digitalis. Following the administration of full therapeutic doses of digitalis (or strophanthin) to dogs, there occurred a fall in right auricular pressure and a rise in arterial pressure, with a simultaneous rise in portal vein pressure. An increase in the volume of the liver and spleen was present, due to constriction of the smooth muscle fibers of the hepatic veins and consequent pooling of blood in these viscera. By this mechanism can be explained the diminution in cardiac output which attends the administration of therapeutic doses of digitalis in normal man and experimental animals, since a diminished venous return gives rise to deficient cardiac filling. In congestive failure, however, the hepatic vein constriction effected by digitalization is believed to relieve the stagnation of blood in the heart and the vascular system, and with a simultaneous increase in systolic ef-

iciency (also due to digitalis) there results an increase in cardiac output with subsequent clinical improvement.

G. H. Miller (J. Clin. Investigation 10:183 (Apr. 20) 1931) has found that the ascitic fluids of certain patients under treatment with digitalis for cardiac decompensation contain a digitalis-like substance. The amount of drug present in these cases is sufficient to be of clinical significance if it were to enter the blood stream. In view of this fact, in treating patients with congestive heart failure with large fluid accumulations, it would seem best not to exceed by too great an extent the full estimated therapeutic dose.

After careful observations on approximately 800 ambulatory patients with auricular fibrillation in the Adult Cardiac Clinic of Bellevue Hospital, H. Gold and A. C. DeGraff (J. A. M. A. 95:1237 (Oct. 25) 1930) found that a much lower "effective concentration" of digitalis in the body is necessary to produce full therapeutic effects in the average ambulatory patient with *moderate* heart failure than is required in the average bedridden patient in advanced congestive failure. In the *average* ambulatory patient with auricular fibrillation it is possible to obtain full therapeutic effects (definite clinical improvement) by daily repetition of a relatively small dose of digitalis (from 2 to 6 grains—0.3 to 0.4 Gm.—of the powdered leaf), which can then be continued for months as the daily maintenance dose without producing toxic symptoms. On the other hand, in patients with far advanced congestive failure larger doses are necessary to obtain benefit, the amount not uncommonly being the largest that can be tolerated without toxic symptoms. In the latter patients (with far advanced failure), the margin

between the maximum amount that can be tolerated without toxic symptoms and the minimum dosage necessary to produce full therapeutic effects is smaller than in the average ambulatory patient, and, therefore, toxic effects are more liable to be precipitated in the former than in the latter through the physician's eagerness to effect prompt improvement in circulatory efficiency [At times, in cases of severe congestive failure, it is most difficult to differentiate between gastric symptoms due to splanchnic congestion and those resulting from overdigitalization. If the full therapeutic dose (calculated by the Eggleston body-weight method) has been given when vomiting occurs, the administration of the drug should be entirely suspended for at least 24 to 48 hours until the symptoms of toxicity disappear. On the other hand, when absolutely certain that vomiting is not due to digitalis overdosage, the drug should be administered hypodermically or by rectum until administration by mouth is possible—ED ]

The authors point out that the "effective concentration" of the drug within the body necessary to *maintain* the full therapeutic effects is usually much lower than that required to produce them in the first place [In determining the daily maintenance dose of digitalis, it is well to bear in mind that the *average* amount of digitalis effect which disappears from the body each 24 hours in the realm of therapeutic effectiveness has been estimated to be 2.25 grains (0.15 Gm) of the powdered leaf (22.5 minims—1.4 cc—of tincture). Because of differences in individual susceptibility to the drug, in the absorptive powers of different individuals, and in physical activities, each patient presents an individual problem. The optimum

daily maintenance dosage for each patient, therefore, can be determined only through trial and careful observation over a period of time—ED ]

To determine the precise stage of optimum digitalization is difficult. If a patient with auricular fibrillation with marked dyspnea, edema of the legs, and a ventricular rate of 140 per minute is given a daily dose of  $4\frac{1}{2}$  grains (0.3 Gm) of digitalis, and after 10 or 15 days the shortness of breath and the edema disappear, the ventricular rate drops to a normal level of 75 to 80 per minute, the patient resumes his work, and the state of improvement is maintained for several months, it is assumed that the full therapeutic effects have been produced, provided no greater improvement is in evidence when the dose is increased. However, when similar results are obtained in the same patient by a daily dose of 3 (0.2 Gm) instead of  $4\frac{1}{2}$  grains (0.3 Gm), the question arises whether the smaller dose will be just as effective as the larger one in preventing the recurrence of heart failure in the course of years. In the present state of knowledge, it is most logical to follow the principle of digitalis dosage suggested by Withering, which is not to give as much digitalis as patients can tolerate without toxic symptoms, but only as much as is necessary to obtain full therapeutic effects, judged by the ordinary signs of clinical improvement.

*Digitalis in Pneumonia.*—For a number of years digitalis has been used quite extensively in the treatment of pneumonia because of the "cardiac support" believed to be afforded thereby. Recently, the value of the drug in this disease was studied in a carefully controlled series of 834 cases of pneumonia in Bellevue Hospital, New York City (W. L. Niles and J. Wyckoff. Tr. A

Am Physicians 45 57, 1930, Am J M Sc 180 348 (Sept) 1930, J Wyckoff, E F Dubois and I O Woodruff J A M A 95 1243 (Oct 25) 1930) Through simultaneous observations made under identical conditions on similarly selected groups of patients treated with digitalis and of patients not given digitalis, no evidence was found to substantiate the conception that the mortality rate in lobar pneumonia is reduced by routine digitalization. In fact, in all categories, with the exception of patients with Type II pneumonia, the mortality rate was increased among the patients who received digitalis. Very striking is the fact that even in a small group of patients with auricular fibrillation, the mortality rate was higher among those receiving digitalis. The mortality rate varied directly with the total dosage, and not infrequently death occurred without any of the usual signs of digitalis toxicity [The value of digitalis therapy in pneumonia is still open to question, however, in view of the evidence presented in this detailed study, the use of the drug should be limited to the patients presenting auricular fibrillation, auricular flutter, or congestive failure. Administration of divided doses only should be recommended, since massive doses have proved distinctly dangerous—Ed.]

In the study of digitalis in pneumonia just discussed, one of the preparations of digitalis used was found to be twice as potent as stated by the manufacturers. J Wyckoff, H Gold and J G Travell (Am Heart J 5 401 (Apr) 1930) point out the vital importance of an exact knowledge of the brand of digitalis when employing the rapid method of digitalization.

In a study of patients with rheumatic heart disease, S Weiss and L B Ellis

(J Clin Investigation 8 435 (Apr) 1930) observed definite clinical improvement during the administration of digitalis, but no significant change could be detected in the cardiac output, the velocity of blood flow, the circulating blood volume, and the vital capacity.

E P Boas (Am Heart J 6 788 (Aug) 1931) calls attention to the fact that, in the absence of organic lesions of the conducting system, the ventricular rate in auricular fibrillation is determined by vagus-accelerator balance, fast and labile rates being associated with preponderant sympathetic action. Much larger doses of digitalis are, therefore, required to slow and stabilize the ventricular rate of patients in whom accelerator influences predominate than in those with a preponderant vagus activity. This factor of nervous regulation—"vagus-accelerator balance"—is of equal, if not greater, importance than body-weight in determining digitalis dosage. Auricular fibrillation with exaggerated accelerator activity is encountered most frequently in the following conditions: (a) Childhood, (b) fever, (c) neurocirculatory asthenia, (d) Graves's disease, and (e) severe cardiac insufficiency. In these patients quantities of digitalis sufficient to produce satisfactory ventricular slowing when at rest are quite apt to prove inadequate when they are up and about. For example, the ventricular rate of a man with mitral stenosis and auricular fibrillation may range from 75 to 85 a minute while at rest, but slight exertion, such as eating breakfast, may elevate it to 125. To such patients enough digitalis must be given to reduce the ventricular rate at rest from 50 to 60 per minute, in order to prevent undue acceleration when they resume their ordinary activities. These patients rarely show

evidence of toxicity before a well-marked slowing of the ventricles occurs, however, with the exceptionally large doses of the drug necessitated, the patient should be kept under continuous observation to guard against possible overdosage as manifested by nausea, vomiting, or bigeminy. In general, the greater the original dose required to slow the ventricles, the larger the maintenance dose; however, the exact maintenance dose can be established only by actual trial in each case.

**Heart Hormones.**—A so-called "heart hormone," with the name of *eutonon*, is recommended by G. Zuelzer (Med. Klin 26 695 (May 9) 1930). The substance is prepared from heart muscle and liver. Six or 8 injections daily are necessary, since the effect is very temporary. It is of value in any of the following conditions: (a) As a prophylactic in normal hearts, and during acute infections which are liable to damage the heart, (b) to improve cardiac reserve preoperatively; (c) to increase exercise tolerance of athletes, (d) to improve cardiac insufficiency, relieving dyspnea rapidly, but having no effect on edema; (e) to relieve angina pectoris; (f) to diminish hypertension, and to elevate low blood-pressure.

**Quinidine.**—See Cardiac Arrhythmias, and Thyroid and Heart Disease.

**Theocalcin.**—H. J. Stewart (J Clin. Investigation 8:389 (Apr) 1930) found marked diuresis to attend the administration of theocalcin in doses of 1.0 to 1.5 Gm. (15 to 23 grains), 3 times daily, in the majority of patients suffering from congestive heart failure. The drug was effective when other therapeutic agents had failed, and it appeared to be more effective and more easily tolerated than theocin and diuretin. Toxic symptoms (nausea and

vomiting) occurred infrequently during its administration, and were but transient. Diuresis usually began during the first 24 hours, but the maximum might not be attained until after several days of administration. The drug can be given as long as it maintains the output of urine near the fluid intake.

### CATARACT.—ETIOLOGY.—

In a study of the nonsurgical treatment of cataract, D. B. Kirby (Arch Ophth 5:856 (June) 1931) investigated the *calcium metabolism* with regard to the relation of calcium to the eye and particularly to the lens and cataract. It is known that calcium is greatly increased in the lens in senile cataract and that calcium deficiency in cases of infantile tetany is undoubtedly responsible for the development of cataract in these cases. Once changes in the labile colloidal solution of the lens protein are established, the administration of calcium or parathyroid extract does not restore the normal state of the protein. No variation in the serum calcium could be found according to age, sex, type of cataract, visual quotient or complicating ocular or general disease in cases of senile cataract. Parathyroid extract-Collip produced excess urinary excretion of calcium, but the excess calcium undoubtedly came from the normal storehouse, the bony trabeculae, and not from deposits in the cataracts.

From a review of the literature and from 4 cases which they describe, T. B. Holloway and A. Cowan (Am. J. Ophth. 14:189 (Mar) 1931) conclude that patients exhibiting disturbances of the zonular lamella of the anterior lens capsule have with few exceptions been exposed to undue and prolonged *heat*.

E. K. Evans and R. Kern (Am. J. Ophth. 14:1029 (Oct.) 1931) made a



chemical study of a number of normal dogs' lenses and of parathyroid cataract lenses produced experimentally in dogs and found an increase in calcium and a decrease of potassium in the parathyroid cataractous lens, similar to that which occurs in senile cataract. They feel that serious consideration should be given the *parathyroid gland dysfunction* in the etiology of *senile cataract* because of this apparent similarity

From their series of experiments with 48 young albino rats, receiving a diet deficient in *vitamin G*, P. L. Day, W. C. Langston and C. S. O'Brien (Am J. Ophth 14:1005 (Oct) 1931) conclude that the absence of this vitamin was responsible for the cataracts which formed in 2 or 3 months. It is interesting to note that further progress of cataract changes was immediately stopped by the feeding of autoclaved yeast which has a high vitamin G content

In India cataract is probably more common than in any other country. Many cases of cataract are the result of insufficient and probably *improper nourishment* as pointed out by J. E. Weeks (J. A. M. A. 94:463 (Feb. 8) 1930). Many Indians restrict their diet to certain foods and omit animal proteins almost entirely. Certain vitamins also may be wanting. The abiotic effect of the shorter light waves on the tissues of the crystalline lens has been clearly demonstrated by the admirable research work of Duke-Elders. It is very difficult to estimate the effect of light waves on the crystalline lens in the ordinary vocations of life. The causative effect of *light and heat waves* in the production of cataract in certain vocations is, of course, recognized. The worker with mercury vapor lamps, short wave light, glass blowers and iron workers, red and other parts of the

spectrum and heat waves, are among those likely to be affected

In India true diabetic cataract is very rare, although cataract with diabetes in general is not uncommon. *Ergot poisoning* is of importance as an etiological factor in the occurrence of cataract. Kortner observed 500 cases of poisoning in which 37 patients had developed cataract, the age of these patients ranging from 6 to 54 years. Opacity in the lens began in the nucleus and spread to the periphery; the cataracts that developed in young individuals matured in from 2 to 3 months, whereas in adults they matured in from 8 to 12 months. With ergotism of the spasmodic and gangrenous types, violent spasms and cramps, with subsequent contraction, occur which affects nonstriated muscular tissue especially. During the spasms the fundus of the eye becomes pallid, while in the interval it may be hyperemic. The formation of cataracts in these cases is attributed to interference of the nutrition of the crystalline lens due to spasm of the intra-ocular blood-vessels

**PATHOLOGY.**—Chemical analysis of the blood in a series of 54 patients with cataract, observed by C. S. O'Brien and V. C. Myers (Arch. Int. Med. 42:376 (Sept.) 1928) revealed that the blood was essentially normal except for the cholesterol content, which was somewhat increased in over 54 per cent. of the cases.

That the lens has a definite protein metabolism and also a definite though small carbohydrate metabolism has been proven by the work of Jess and Warburg. After investigating the nature of the lens capsule by determining what substances can diffuse through it, and whether or not a sufficient alteration in the permeability of the capsule takes

place to interfere with the lens metabolism, thereby causing cataract, J S Friedenwald (Arch Ophth 3 182 (Feb) 1930) concluded that (1) all electrolytes and true water solutes may permeate the capsule, (2) the capsule acts as a semipermeable membrane and its permeability is decreased by calcium, cyanides and proteins, (3) the permeability of the capsule varies in individuals but not in species, and the permeability is greater in young animals than in old ones, (4) exposure of the capsule to the action of cataractous lens cortex increases its permeability

**TREATMENT.—Nonoperative.**—M E Marcove (Am J Ophth 14 887 (Sept) 1931) reports a case in which lenticular opacities developed in a patient in tetany following thyroidectomy for exophthalmic goiter. Treatment with calcium and parahormone arrested the development of lens changes and resulted in the disappearance of the symptoms

In a series of senile cataract cases treated with injections of parathyroid extract—Collip, D B. Kirby (Arch. Ophth 5 754 (May) 1931) observed no improvement in the vision, refraction, or objective appearance of the cataracts. He believes that parathyroid extract may be of value in cases of deficiency in calcium in which calcium and parathyroid therapy are indicated

E Ginestous (Gaz Hebdomadaire de Bordeaux 152 (Mar 10) 1929) reports that in more than 50 cases of incipient, diabetic and senile cataract treated by the local use of sulphur, the opacities not only did not progress but showed regression. He employs the following formula: precipitate sulphur, 0.1 Gm ( $1\frac{1}{2}$  grains); oil of sweet almonds, 2 Gm (30 grains); crystallized calcium chloride and dried so-

dium iodide,  $\bar{a}\bar{a}$  0.4 Gm (6 grains), neutral vaseline and lanoline,  $\bar{a}\bar{a}$ . 5 Gm ( $1\frac{1}{4}$  drams). A piece the size of a pea is put into the eye morning and night. This treatment is useless in congenital, traumatic or old cataracts, but is beneficial in *diabetic* and *senile forms*

**Surgical Treatment.**—C C O'Malley (Brit J Ophth 15 152 (Mar) 1931) operated upon about 200 cataracts while in India. He describes the technique of the Smith **intracapsular operation** as done by Das and believes this operation is better than any of the others

A high percentage of good results is reported by A. E. Edgerton (Am. J Ophth 14 1039 (Oct) 1931) in 950 cataract operations in which the **intracapsular operation** was the operation of choice, performed during a month's service with Dr Holland, at Shikarpur, India. More than half of the cases were bilateral extractions.

From his results in 540 cases of **intracapsular extraction** M. I. Puiggari (Semana médica 1 876, 1931) concludes that because of the anesthesia by retrobulbar injection and conjunctival instillation, and immobility of the eye, which are now obtainable, the intracapsular operation can be performed without danger. He believes it will become the method of choice because of its quick and excellent results and because it is not followed by secondary cataract, and, therefore, can be used for immature cataract. The author believes that **peripheral iridectomy** or **iridotomy** should be performed.

A Hess small **marginal iridectomy** is advocated by A. J. Manes (Semana médica. 1 941 (Apr. 9) 1931) in order to avoid danger of injury to the lens or the hyaloid membrane, in **intracapsular extraction**. This leaves the sphincter

of the iris intact. He recommends retrobulbar injection which causes a hypotension, by the action of the injection on the ciliary ganglion which affects the ciliary body through the sympathetic innervation. If incarceration of the iris is found within 24 hours after the operation, another retrobulbar injection and a myotic mixture of **pilocarpine** and **eserine** are given and **heat** applied by means of an **electrical thermophore**. He advises operating as soon as the pupils are satisfactorily, but not excessively, dilated.

In his report of a third series of 100 successive **intracapsular extractions after preliminary subluxation** with capsular forceps, A. Knapp (Arch Ophth 5:575 (Apr) 1931) lists the *contraindications* to this method as follows: (1) Prominent eyes, (2) myopic eyes, (3) soft eyes, (4) cyclitis eyes; (5) complications due to vitreous disturbances; (6) cataract in persons under 50 years of age; (7) Morgagnian cataract, (8) nervousness and restlessness.

A large scleral section, especially in undersized eyes, is advisable. In his series of 100 cases Knapp found the cataract mature in 40, nuclear and posterior cortical in 27, complicated in 15, hypermature in 15, and of the Morgagnian type in 3.

A modification of the technics of **Barraquer and Green** for cataract **extraction** is described by O. R. Wolfe (Am J. Ophth 14:510 (June) 1931). He dissects a large circular conjunctival flap from above and on the sides and then places 2 sutures on the sides. Experience with **phacoeresis** in 200 cases during a period of 7 years presented no instance in which vitreous was lost as a result of suction.

W. B. Lancaster (Surg Gynec Obst

52:452 (Feb—No 2 A) 1931) advocates the following points in his technic for cataract operation: (1) Double fixation of the eyeball by means of forceps, (2) a stitch through the superior rectus, (3) good **local anesthesia** supplemented by the use of large amounts of **barbital**, **sodium amytal**, **codeine** or **hyoscine**; (4) a large corneal section made parallel with the iris and behind the limbus, (5) a conjunctival flap, (6) intracapsular extraction by simultaneous external pressure below the limbus and traction with the capsule forceps to dislocate the lens, (7) a buttonhole iridectomy in most cases.

### CEREBRAL CIRCULATION.

—W. G. Lennox and E. Leonhardt (Arch Neurol and Psychiat 26:719 (Oct) 1931) determined the respiratory quotient of the brain by removing blood simultaneously from the carotid artery and jugular vein in man. They find that the average respiratory quotient of 0.82 as determined for the entire body is composed of values which vary greatly in the different tissues of the body. They found the respiratory quotient of the brain to be 0.95, whereas the arm gave values of 0.86 and the leg 0.72. The findings indicate that ectodermal tissues (the brain and skin) are higher in their needs for oxygen than the muscles, and other organs of the body. Incidentally, they determined that more dextrose disappears from the blood as it passes through the brain than in that which passes through the extremities.

These studies have a practical significance in that the brain requires a far higher degree of oxygen for function than other tissues and that in the presence of a general deficiency in the supply of oxygen, cerebral symptoms of

anoxemia might be expected to occur early, and conversely, the damage incurred by periods of the loss of oxygen affect the nervous tissues to a greater degree than other organs

#### EFFECT OF MENTAL WORK.

—W. G. Lennox and E. Leonhardt (Arch Neurol and Psychiat 26 725 (Oct) 1931) extend their studies in cerebral circulation to include oxygen determinations from the jugular veins and carotid arteries in the human being during periods of rest and of mental activity (arithmetic problems). Their studies clearly indicated that with the advent of mental activity, the average oxygen content of the blood was increased 13 per cent by volume. They explain their results on the basis of dilatation of the cerebral vessels, with the resultant increase of speed of the blood flow through the brain, and bring out the interesting question as to whether mental defectiveness may be related to the readiness with which the cerebral circulation responds to mental effort. The importance of this work is self-evident, and may throw a great deal of light upon not only variations in mental activity in the normal, but indicates that a high degree of vascularity of the brain may follow mental effort, and the consequences of thought and emotional processes which can readily disturb the volume relationships within the skull to such a degree that headache and other symptoms may result.

Lennox and Leonhardt (*Ibid.*) refrain from drawing any conclusions as to the possible results of this work in clinical practice, but those who have followed the investigations of Lennox, realize that many important considerations have arisen from investigations of this nature. Their observations suggest the solution of numerous practical problems

**CARBON DIOXIDE AND OXYGEN INHALATIONS.**—S. Cobb and Fremont-Smith (Arch Neurol and Psychiat 26 731 (Oct) 1931) present important evidence to show that a mixture of 90 per cent oxygen and 10 per cent carbon dioxide increases the diameter of the arteries in the retinal circulation by inducing a condition of acidosis, thus favoring a more rapid dissociation of oxygen from the hemoglobin, and makes more oxygen available for the tissues. They found that this mixture stimulates respirations and increases blood-pressure. They determined by a color index the changes in the retinal veins and found that with the inhalation of the above mixture, the veins became bright red and resembled the arteries, which they believe to be due to the wide-opening of the arterials, permitting blood to flow so rapidly through the capillary bed that it loses no appreciable amount of oxygen. The marked beneficial effect of such a mixture has been noted in catatonic stupor, Parkinson's disease and other lethargic states. Patients have been dramatically awakened, probably due to a more efficient and active supply of oxygen to the brain cells. The authors suggest the possibility that chronic encephalitis might be due to hypoxemia of the nerve cells, causing first functional deficiency and finally necrobiosis.

The importance of this contribution may well be realized in those cases where arousal from stupor becomes necessary, or for chronic lethargic states where better cerebral circulation is desirable. Although the response is temporary to such a mixture, the value of these observations in surgery at a time when emergency measures are required, gives a method of treatment which may be effectual in **morphine poisoning**,

and temporary cerebral circulatory collapse.

**EFFECT OF HISTAMINE.**—S Weiss and W G Lennox (Arch Neurol and Psychiat. 26 737 (Oct) 1931) show by careful measurement of oxygen and carbon ratios in the jugular and carotid vessels that the minute cerebral blood-vessels in man respond with dilatation to histamine, and that the sensitivity of the human cerebral arterials is usually great to histamine. The findings indicate that chemical substances acting locally may play a rôle in the physiological and pathological cerebral circulation in man. The toxic effect of traumatic injuries, at a distance, conveying by-products similar to histamine, may be expected to produce circulatory changes in the brain. The so-called toxic effects encountered in burns and severe crushing injuries to the extremities, as well as extensive surgical procedures involving large masses of tissue destruction may be a source for such cerebral changes.

**CEREBROSPINAL FLUID.—EXPERIMENTAL PHYSIOLOGY.**—The method of study of the cerebrospinal circulation used by E. Sachs, H. Wilkins, and C. F. Sams (Arch Neurol and Psychiat. 23.130 (Jan) 1930) consisted in the injection of trypan blue into the closed sub-arachnoid space and then observance of the distribution of the fluid color. Two hundred milligrams of trypan blue dissolved in 1 to 1.5 c c of isotonic saline or cerebrospinal fluid were used. Specific gravity of the fluid before the dye was added was 1.007, and with the dye in colloidal suspension it was 1.025. In order that no alteration of pressure would be affected 0.5 c c of the colloidal suspension was drawn into a

syringe, then 0.5 c c of cerebrospinal fluid was drawn in. Following injection, the total volume of fluid in the cerebrospinal system was unaltered, as was the intradural pressure.

These investigators believe there is no true circulation of the cerebrospinal fluid. Substances spread in the cerebrospinal fluid by diffusion; this diffusion process being influenced by gravity. No evidence is at hand that oscillations in the fluid, due to pulse and respiration, play any rôle in the movement of cerebrospinal fluid. Reduction of pressure on lumbar puncture causes an artificial circulation toward the point of puncture. This is of great importance from the clinical viewpoint. If it is desired to inject serum with the idea of it reaching all parts of the nervous system, it is much more valuable to make use of gravity by injecting it into the ventricles or basal cisterna than to inject it into the lumbar meninges. With meningitis present, repeated withdrawals of fluid by spinal puncture or permanent lumbar drainage tend to spread the infection by producing an artificial circulation. If drainage is indicated, it should be done in the region of the basal cisterna as recommended by Dandy, rather than from the lumbar region. Since a substance of the same specific gravity as the cerebrospinal fluid diffuses at a slow rate, it is suggested, in order to get the greatest effect from the serum, to administer it by cisternal puncture or ventricular puncture unless the process has already extended into the lumbar spaces.

When the veins in the neck are compressed, pressure of the cerebrospinal fluid increases rapidly. Increased pressure, according to A. Pometta (Schweiz. med. Wchnschr. 60.773 (Aug 16) 1930), should cause pain at the point

where a disease process is located. From detailed observations on 1 patient he concludes that it is possible to produce pain where a pathologic process is located within the spinal fluid or in its surroundings. The reaction is said to occur several minutes after an elastic tourniquet has been applied, the pain increasing gradually and subsiding after the tourniquet is removed. This tourniquet should be applied to the neck for not less than 5 to 8 minutes and the pressure should not be excessive. Positive reactions only are of diagnostic value. Not all pathologic symptoms will react to the test, it should be helpful, however, in conditions such as tabes, sciatica, tumors of the spine, coccygodynia and acroparesthesia. The test is contraindicated in advanced hypertension, in cerebral tumors, arteriosclerosis, and in acute meningitis.

**PATHOLOGY.**—Examination of 100 cerebrospinal fluids by W. J. Penfold and D. H. Irving (Med. J. Australia 1:772 (June 14) 1930) revealed the average quantity of each constituent present as follows: protein, 24 mg per 100 cc; chloride, 732 mg; sugar, 76 mg; urea, 24 mg. The lowest sugar content found was 68 mg.

A study of the *proteins* in the cerebrospinal fluid is of importance not only for the purpose of diagnosis but also for the guidance of treatment. A *colorimetric method* for the determination of the spinal fluid protein has been devised and advocated by P. B. Matz and N. Novick (J. Lab. and Clin. Med. 15:370 (Jan.) 1930), by which the quantities of globulin and total protein may be estimated, and the amount of albumin present determined by deducting the amount of globulin from the total protein. The average ratio of albumin to globulin was 2.6:1. The

average quantities per 100 cc of the various proteins of spinal fluid in untreated cases of *paresis* were as follows: albumin, 65 mg; globulin, 44 mg; total protein, 110 mg; the average albumin globulin ratio being 1.5:1. The average quantities per 100 cc of the various proteins in the spinal fluid in *tabes dorsalis* were as follows: albumin, 42 mg; globulin, 16 mg; total protein, 62 mg; and the albumin globulin ratio 2.1:1. The average quantities per 100 cc of spinal fluid of the various proteins of cases of *tertiary syphilis* were as follows: albumin, 45 mg; globulin, 16 mg; total protein, 61 mg. The average ratio albumin to globulin 2.9:1.

It is noted, therefore, that the quantities of the various proteins of cerebrospinal fluid of tertiary syphilis with apparent involvement of the central nervous system were slightly in excess of the quantities of the proteins in non-meningitic and non-luetic fluids.

With *multiple sclerosis* the average quantities of the various proteins per 100 cc were: albumin, 71 mg; globulin, 33 mg; total protein, 104 mg; and the average ratio of albumin globulin was 2.2:1.

A study of the proteins of the cerebrospinal fluid of several cases of *paresis* undergoing treatment revealed that during treatment a reduction of the albumin fraction took place. The globulin content was not influenced as readily as the albumin. The ratio of albumin to globulin varied in more than half of the cases.

Improvement clinically should be followed by an increase of the albumin to globulin ratio. The decrease was evidently due to the fact that the albumin fraction was more greatly influenced by treatment than was the globulin fraction.



The smallest quantities of the various proteins were found in the nonmeningitic and nonsyphilitic fluids, while the largest quantities were noted in paresis and multiple sclerosis. The ratio of albumin to globulin was high in the nonmeningitic and nonsyphilitic fluids. The lowest ratio of albumin to globulin was found in paresis.

Following a survey of the literature, B. S. Walker and F. H. Sleeper (Am J Psychiat 10:229 (Sept) 1930) came to the following conclusions: (1) A strongly positive *Boltz reaction* is given in about 95 per cent of all cases of cerebrospinal fluid from untreated patients with *dementia paralytica*, (2) positive reactions are obtained in numerous other affections, whether or not syphilis exists, (3) in *neurosyphilis*, treatment tends gradually to reduce the intensity of the reaction, (4) in cases in which protein has also been determined, the intensity of the Boltz reaction varies with the protein content. In fact, it is obvious that the Boltz reaction is not in any way specific as a diagnostic aid for neurosyphilis. As a means of rapidly determining the amount of protein in the spinal fluid, it seems to be of value. It is also doubtful if the test can ever be made really quantitative even by the use of color standard and controlled time and temperature. The color is transient, the reagent (glyoxylic acid) is unstable, and the test is apparently subject to interference from other substances in the fluid, such as an excess of dextrose.

Determination of the *refractive index* of the cerebrospinal fluid appears to furnish possibilities in the diagnosis of certain diseases. A series of normal and diseased fluids were examined by W. J. Penfold and C. A. E. Price (Med J Australia 2:424 (Sept 28) 1929)

using a Zeiss dipping refractometer with an accessory prism for examination. Observations were made at a temperature of 17.5° C in a water bath and were always read in daylight.

In normal adult spinal fluid the average reading was found to be 1.334<sup>10</sup> and much less variation existed between high and low limits than in other body fluids. The average reading for 7 children was 1.335<sup>08</sup>. A marked rise in protein concentration is associated with a rise in the index, while a moderate rise may not be found with a rise in the index because of the compensating effect of an accompanying fall in the chlorides.

Deviations exceeding 0.00008 above or below the normal are pathological. A definite rise in the index occurs with *uremia* and *diabetic coma*. *Meningitis* usually shows a high index. With *intracranial tumors*, the index is normal or raised, and with *encephalitis* and *anterior poliomyelitis*, the refractive index is practically normal. *Spinal block* is easily detected by comparing the indices of cisternal and lumbar fluids. The use of the index as a check on the chemical analysis of the fluid is of importance.

The relationship between the cerebrospinal fluid and the *body temperature* was studied by A. Gordon (Rev Neurol 2:44 (July) 1929) in 250 patients, *i.e.*, 25 with hemiplegia, 5 of which had symptoms of intracranial hypertension; 17 cases of epilepsy; 10 of meningitis; 40 of neurosis, 12 of manic-depressive psychosis, 10 of transverse myelitis; 20 of tabes; 4 dementia precox, and 40 of intense headache of luetic origin. Of the spinal fluid from children, 10 were from patients with meningitis, 15 mentally deficient cases, 20 epileptics, and 5 cases of Little's disease. A withdrawal of spinal fluid produced a rise in temperature proportional to the

amount of the fluid withdrawn. In the children the effect was similar to the one in adults except that the rise in temperature was greater. When the puncture was unsuccessful and fluid was not withdrawn, the temperature remained the same, even if puncture was repeatedly attempted.

In some patients in whom irritations of the meninges existed, withdrawal of purulent cerebrospinal fluid was followed by the customary therapy of injection of physiologic saline, and in these an instantaneous lowering of the temperature occurred, followed, however, by a considerable rise. In several patients in whom ventricular puncture was performed and fluid withdrawn and replaced by an equivalent amount of air or physiologic saline, a greater rise in temperature occurred than those in whom this substitution was not made.

The rise was greater in manic-depressive psychosis and in psychoneurosis, and in the former it was higher in the maniacal attack than during the period of depression. The mechanism determining these phenomena, according to Gordon, is located in the tissue enclosing the ventricles, probably of the third ventricle. The changes in the configuration of the ventricles caused by the withdrawal of the cerebrospinal fluid produce an irritation of the blood-vessels and the nerve endings located in the walls and thus cause a change of body temperature.

**CHARCOAL.—THERAPEUTICS.**—H. Nahmmacher (Surg. Gynec. Obst. 50: 873 (May) 1930) has advanced the use of pencils of granulated charcoal measuring 3 to 5 cm. in length and 4 to 5 mm. in thickness in **intrauterine infections** due to abortions, either before or after complete

emptying of the uterus, in **puerperal endometritis**, and in cases of Cesarean section in which the membranes have been ruptured for some time. He believes that the intrauterine use of charcoal is practically without danger and his experience showed that the symptoms are instantaneously influenced for the better, since there is an immediate improvement in the general condition of the patient and in the local inflammatory reaction, signified by a fall in the temperature and pulse rate.

**CHEMOTHERAPY.**—The principles of the use of chemotherapeutic agents, are commented upon by R. A. Kilduffe (J. Chemotherapy 6: 79 (Jan) 1930), who states that they act in 2 ways, *i e*, (1) on the bacteria concerned and (2) on the tissues of the body, and that the dosage and type of drug must be based upon both actions. He is quite firmly convinced that in profound bacteremia it is not always advisable to attempt to clear up the blood stream entirely with 1 massive dose of the drug, despite the fact that a sufficient amount might be given and still not cause harm to the tissues. He bases this belief upon the fact that disintegrating bacteria release an endotoxin which is irritating to the system and, if released in sufficient amount at one time, might cause such severe damage as to defeat the purpose desired. He feels that all intravenous chemical medication should be regulated by careful study of the blood stream by culture, with determination of the number and type of bacteria per cubic centimeter of blood. He also feels that no intravenous chemical therapy is warranted without at the same time making an attempt to clear up an original focus and any secondary foci that may have formed through embolic action. Kil-

diffe strongly stresses the need of early and immediate recognition of blood stream conditions in order to obtain the best results in chemotherapy

P Spanier (Beitr z Klin d Tuberk. 73 210 (Dec 18) 1929) describes numerous experiments on animals in which it was shown that in lung infections the leukocytes pick up the chemical product from the blood stream and carry it to the lungs, where it comes in contact with the infected tissue and produces its action while the leukocytes are temporarily present. In all cases, the leukocytes act simply as a mechanical carrier for the drug.

**CHEST INJURIES.**—Attention is drawn by D S Allen (Arch. Surg 21: 1161 (pt 2) (Dec) 1930) to the difference in the fundamental principles of treatment in *pleural* and *peritoneal injuries*. The treatment for wounds that penetrate the peritoneal cavity usually is radically operative; for those which penetrate the thoracic cavity, the conservative nonoperative treatment is often the best. The presence of blood within the abdominal cavity is of little moment. It may be left undisturbed. Blood left within the pleural cavity may lead to extensive empyema and death. If the surgeon performs an exploratory thoracotomy on the same premise as he does an exploratory laparotomy, for example, for a penetrating gunshot wound, many patients whose chests are explored will die who otherwise would not have died.

The explanations for this are based on 5 facts (1) There are differences in the organs contained in the pleuræ, and those within the abdominal cavity. (2) The pressures within the pleural cavity are maintained at a more negative level than are the pressures within

the abdominal cavity. The natural tendency of the pleural cavity is toward the formation of cavities, the natural tendency of the abdominal cavity is toward their obliteration. (3) The pleural cavity seems to react to the presence of contaminated blood in a manner different to that of the peritoneal cavity. (4) It is impossible to bring the pleural cavities and the organs that they contain to a complete or even an effectual rest. (5) The blood-pressure within the pulmonary circulation is only one-sixth the pressure within the general circulation; bleeding is more easily controlled when it occurs from the pulmonary system than when it occurs within the abdominal cavity.

The considerable difference in the average wounds of civil life and those of war, accounts for the rather different handling of many, but the underlying principles in all are the same. Where the chest traumatism of civil life approaches in severity the high explosive war injuries, the treatment must be the same; the low incidence, however, of such gross thoracic injuries makes radical and extensive chest surgery less frequently necessary.

Allen (*loc cit.*) bases his study on 162 gunshot and stab cases seen in Barnes 2d—St. Louis City Hospital. With 2 exceptions they were all recent cases. Of 47 stab cases, 7 were fatal, but no patient died of lung injury, the fatalities occurring in 5 with associated abdominal injuries and 2 with heart penetration.

In the 115 gunshot wounds only 5 died when the gunshot wound involved the chest alone. Two of these died immediately of hemorrhage, and 3 died later as a result of infection of the pleural cavity and injured lung. Another 22 died who had major injuries.

Since the great danger in these cases lies in infection of a *hemothorax*, particular attention was directed to the handling of this complication, and the basic principle of aspiration met in a new way. He says "There is a more simple way of removing the blood from the pleural cavity than by aspiration. It consists of *closing of the wound in the wall of the chest and having the patient lie with the closed hole down in the most dependent portion of the chest*. The hemothorax will gradually leak out. This procedure was used as a routine measure in 39 cases. None of the patients died. In 6 of the 39 cases sufficient blood remained in the pleural cavity to justify aspiration."

The question is raised as to whether early evacuation of blood in hemothorax may not favor continuation of bleeding by releasing the compression which experience has found to be so effectual in control of pulmonary hemorrhage, but in the group studied there was no evidence that the gradual escape of blood increased or favored recurrence of the hemorrhage. Allen (*Ibid*) believed that it was the very gradual escape of the blood, with corresponding slow pulmonary expansion, which lessened any tendency toward clot displacement from injured vessels as the lung refilled the pleural cavity.

In the discussion of this paper there was agreement that aspiration of hemothorax should not be done immediately. Bazin stated that during his war service he learned that the infection of a hemothorax could be anticipated and dealt with accordingly. The fluid aspirated was spread out on a plate, and little portions of the clot picked out. These were crushed under a cover-slip and stained, and occasionally definite colonies of organisms would be found in those

little clots. As soon as that was discovered the case was ready for operation, **thoracotomy, thorough cleansing of the hemothorax, and complete closure in layers, an airtight closure, with subsequent repeated aspiration.** Massive empyema or any severe infection in the pleural cavity was thus avoided, with the culture medium clot removed it reduced the infection to one of comparatively mild degree.

D. C. Elkins, in the same discussion, spoke of a series of 96 patients with penetrating wounds. Seven died within 12 hours, only 1 after this period. He states that the method of treatment was to give all of the patients large amounts of morphine, to close the external wound when they were "sucking" and to begin aspiration on the third to fifth day, it was considered that if the fluid was left alone that long, it would compress the lung and prevent further bleeding and that after that time there would probably be no bleeding after aspiration. In 3 of the 89 patients who lived, empyema developed, 1 dying of staphylococcic septicemia, the other 2 having a chronic empyema taking considerable time to heal.

**CHLOROFORM.** See ANESTHESIA

**CHLOROSIS.**—J. Damianovich (Arch. argent de pediat 1. 365 (Sept) 1930) made a study of the blood examination of 2 series of infants with chlorosis or chloroanemia—1 group of 3 triplets with probable congenital syphilis and 4 other infants. Chlorosis and chloroanemia have a characteristic clinical and blood picture which affords differentiation from other types of anemias and may be looked upon as a primary stage in the development of alimentary anemia. The principal etiological con-

dition is congenital syphilis, which acts as the predisposing factor, and a prolonged alimentation with milk, the determining factor. Congenital syphilis alone may cause the disease. In infants with pronounced anorexia, when the conditions cannot be determined clinically, changes in the blood formula should be looked for. The treatment includes the proper diet and medication. In infants older than 1 year of age, liver therapy is to be tried, and ultra-violet irradiation should be likewise employed. Vitamines are to be included in the diet. Medical treatment based on the etiological data and the administration of iron oxalate, the oral administration of yellow mercurous iodide, especially when syphilis is proven, or weak solutions of arsenic salts for protracted cases is indicated.

**CHOKED DISC.** See PAPIL-  
EDEMA

**CHOLECYSTOGRAPHY.**—L. R. Whitaker and S. W. Ellsworth (New England J Med 205 1183 (Dec 17) 1931) advise the administration of 2 full doses of tetraiodophenolphthalein, with an interval of 6 to 8 hours, and attempt to prevent the emptying of the gall-bladder by allowing only carbohydrate food between the first and second dose. They believe that the density of the shadow and the reliability of the method are both increased by thus supplying more radio-opaque substance and allowing more time for the concentration of that opaque substance in the gall-bladder.

Small repeated doses of sodium tetraiodophenolphthalein are used by C. Sandstrom (Acta radiol 12 8, 1931) over a period of 2 to 4 days. He obtains denser shadows than are obtained by the usual Graham method. His

theory is that since the drug is slowly eliminated, due to its reabsorption from the bowel, its concentration in the bile is thereby increased. Whitaker and Ellsworth believe that the increased dosage, by Sanderstrom's modification of the Graham method, may be of no advantage, since no provision is made for preventing the emptying of the gall-bladder which follows ordinary meals, and the cathartic action of the drug in some cases causes its rapid elimination. Carbohydrate foods produce no emptying of the gall-bladder. If fats and proteins are avoided after the first dose of the drug, repeated administration should theoretically result in increased concentration in the gall-bladder, even in spite of catharsis.

The essential part of their modification of the Graham method (for preparing the gall-bladder for x-ray, by rendering its contents opaque, if its ducts are patent), is the principle of preventing the emptying of the gall-bladder between doses of the drug.

The usual schedule is as follows. At midday the patient eats an ordinary meal, followed immediately by an average dose (1 dram—4 Gm) of sodium tetraiodophenolphthalein, which has been prepared for oral administration. Water only is taken thereafter until 8 P. M., when a carbohydrate meal is given. An example of a suitable meal is dry toast or white crackers, any fruit or fruit juice, clear tea or coffee and sugar. Following this meal, another dose of the drug, equal to the first, is administered as before, following which only water is allowed until the x-ray study is made on the following morning.

When a very faint shadow, or none at all, results, it is necessary to determine whether the patient took all of the drug prescribed and retained most of it,

whether he ate no fat or protein after the first dose, and whether the patient was not purged severely enough to eliminate too much of the drug

The fatty meal employed by Whitaker and Ellsworth consists of 4 egg yolks,  $\frac{1}{2}$  pint (250 c c) of cream, and ginger ale for flavor

It is important to record the emptying of the gall-bladder after the fatty meal, and exposures should be made often enough to show the reduction of the size of the shadow to the smallest dimensions it achieves. This requires exposures at from half-hourly to hourly intervals. The emptying time of gall-bladders is so variable that it is impossible to formulate a routine which uses only a few films. The negative shadows of small cholesterol stones are often visible only after the amount of opaque material in the gall-bladder has been greatly diminished, so that they may not be seen if an x-ray picture is not made when the gall-bladder has reached the appropriately small size

Useful surgical information may be gleaned by careful observation of the contractability of the gall-bladder. L. R. Whitaker (Am J Surg 13 273 (Aug) 1931) notes that a gall-bladder which has marked ability to contract must have an active musculature, and therefore, can not be severely sclerosed. The serosa can be easily separated from it, and so permit a subserous resection of the gall-bladder

G. Levine and L. R. Whitaker (New England J Med 202:203 (Jan. 30) 1930) suggested a combined intravenous-oral method of administering tetraiodophenolphthalein, but Whitaker and Ellsworth state that the 2 oral doses with the carbohydrate diet and 8 hour interval between them, give results which are always superior in heaviness

of shadow to the old Graham method, and equal to either the intravenous or combined intravenous and oral methods. Their contention is based on a comparative study, by their method, of 50 cases having normal gall-bladders

It is important to recognize the fact that there is a great variability in normal gall-bladders. Experiments have shown that in patients with normal gall-bladders, with repeated tests, the shadows are persistently fainter in some individuals than in others. Therefore, the faintness of the shadow is not, alone, a sufficient criterion of gall-bladder disease

With the usual oral methods, a very faint or absent shadow is sometimes produced with a normal gall-bladder, leading to the erroneous diagnosis of gall-bladder disease, but with the intravenous or "double oral" methods a shadow is produced which can be seen to contract, in the normal gall-bladder, to a very small size following the fatty meal, proving the essential normalcy of that organ

If any small stones are present in a gall-bladder which is well contracted after having been rendered opaque, they will be noted by contrast in the decreased volume of opaque material, unless they are calcium stones, in which case they will be seen on the plain film

There is inconvenience, discomfort and some danger in intravenous administration of the drug, whereas in 50 cases treated with the oral repeated dose method, the shadow has been equally as opaque, with no gastrointestinal reactions of any severity

**CHOLESTERIN.—TREATMENT OF SKIN AND HAIR DISORDERS.**—The product of the sebaceous glands consists of a large part of



cholesterin, and hair depends on this for its nutrition. Cholesterin belongs to the stearyl group. It is present in the white matter of the brain and comprises 20 per cent of its ash. It is also found in the gall-bladder, in the kidney, and in cutaneous secretions as an ester, also in the blood compounds as pure cholesterin.

The cholesterin content of the body changes in certain dermatoses, particularly in xanthomatosis. It has also been shown that with advancing age the cholesterin content of the skin diminishes. A constant hypercholesterinemia is noted in all streptococcic dermatoses. It is also noted in certain types of skin tuberculosis and in psoriasis.

In 200 cases cited, A. Brandweiner and Kunewald (Wien k Wchnschr 43:586 (May 8) 1930) noted an increase in cholesterin blood content in the following skin diseases, eczema, urticaria, psoriasis, pediculosis, pseudo-exanthem, skin tuberculosis, vitiligo, neurofibromatosis and purpura. In skin diseases, including diseases of the hair, and especially in acne, psoriasis and certain forms of defluvium, the intramuscular injection of a mixture of *sulphur*, *eucalyptol* and *cholesterin* produces favorable results.

An ointment containing cholesterin and also an alcoholic solution of cholesterin is recommended in seborrheic type of alopecia.

**CHOREA MINOR. — ETIOLOGY — Predisposing Causes.** — The disease is more common in *girls* than boys, the ratio being 3:1, according to H. M. Fletcher (Practitioner 125:165 (July) 1930) and R. G. Tuck (Clin Med and Surg 37:100 (Feb) 1930). The greater liability of the girls to chorea, as compared with boys, Fletcher believes is probably due to the more

delicately balanced and sensitive nervous system in the female sex. Fletcher states that the disease occurs more frequently in the *urban* than in the rural districts, and in the *lower* than in the upper *classes*. Choreic patients are usually *bright, intelligent* children, not the dunces. Tuck states that chorea seems to be on the increase. It seems certain that the young people of today are subjected to a much greater *nervous tension* than was present a decade ago. The tendency for the greatest *seasonal* incidence of chorea to occur in the spring, Tuck believes, may be due to a lack of sufficient ultraviolet radiation and of a green vegetable diet. Chorea is mainly a disease of childhood. According to Fletcher the disease is rare under the age of 5 years. After the age of 25 years, E. C. Warner (Lancet 1:339 (Feb 15) 1930) states that the disease is rare, except during pregnancy. In other words, Warner points out that chorea is seen during the period of growth, when there is a special need for calcium in all the tissues of the body, and again during pregnancy, when again there is a drain on the calcium reserve of the body. This author states it may be that just as rickets is associated with faulty *calcium metabolism* at an early age, so is chorea at a later age.

Warner (*loc cit.*) examined the blood in 38 cases of chorea and found that there is a rather low value in the total serum *calcium*, which rises as the chorea subsides. The calcium content of the cerebrospinal fluid has been found by Warner to be consistently low, and at the same time he has observed a rise in the electrical excitability of the peripheral nerves and muscles, as measured at the "motor point." As recovery ensues, electric hyperexcitability diminishes, corresponding with the rise in the

calcium content of the cerebrospinal fluid.

**PATHOLOGY.**—J Lhermitte and P Pagniez (*Encéphale* 25 24 (Jan) 1930) report the case of a woman, age 19 years, whose illness began in November and progressed to a typical choreic death in December. Grossly, upon necropsy examination, there was evident congestion of the meninges. Microscopic examination revealed vasodilatation, vascular rupture with capillary hemorrhage, distention of the adventitious sheaths by an albuminous exudation and cellular changes—tigrolysis and karyolysis, with the gradual reduction of the cytoplasm and the final destruction of the cell. The lesions were predominant in the dentate nucleus, putamen caudate segment of the striate body, and the Purkinje cells of the cerebellar cortex. On the basis of these and similar reports, these observers believe that it is reasonable to think of acute chorea as divisible into 2 groups, one characterized by more or less diffuse encephalitic lesions, and the other by a more degenerative type with vascular modification.

**SIGNS.—Respiratory.**—W. Stoeltzner (*Ztschr f. Kinderh* 48 124, 1929) observed that when a child with chorea is asked to take a breath he will open his mouth without inspiring. This response is looked upon as an expression of disturbance of coordination.

**Dorsal Reflex.**—According to G. A. Stephens (*Brit. M. J.* 1 303 (Feb. 21) 1931), hyperesthesia is present on both sides of the spine in chorea patients, extending upward as far as the third dorsal vertebra, and downward to and including the area supplied by the second sacral nerve. There is also a marked *superficial reflex*, the trapezius, latissimus dorsi, and glutei muscles responding readily when the overlying skin is

pricked lightly with a pin. This reflex, the author states, can be demonstrated in nearly every child with chorea.

**Basic Blood-pressure.**—Basic blood-pressure, according to Stephens (*loc cit*) may be defined as that pressure left acting on the blood in the brachial artery, after the systolic pressure has been stopped by the inflated armlet. The normal basic pressure is found to be 50 mm Hg, but in children suffering from chorea, the basic pressure is raised to 70 mm or upward. It follows that in chorea with an increased basic pressure, the supply of poor blood to the walls of the cerebral arteries diminishes the blood in the brain. As a result, the brain cells act irregularly and set up irregular stimuli, producing a corresponding choreic effect on the muscles.

**PROPHYLAXIS.**—A. D. Kaiser (*J. A. M. A.* 95 837 (Sept 20) 1930) studied 2000 children of high-school age, one-half of whom had their tonsils removed at the age of 5 or 6 years. An equal number of children in whom tonsillectomy was recommended 10 years before, but not performed for various reasons, was likewise examined, and served as a control group in the study. Chorea occurred with equal frequency in the 2 groups before operation, but over the 10-year period it occurred twice as often in the operated group. In another survey made on rheumatic manifestations in a much larger group of children, it was found that chorea occurred as often in the children who had been operated as in the control group. The disease does not seem to be favorably influenced by removal of tonsils, except that less carditis is associated with chorea occurring in tonsillectomized children.

**TREATMENT.—Nirvanol.**—(Phenyl-ethyl-hydantoin). B. Schles-

inger (Proc Roy Soc Med 23 468, 1929) recommends a daily dose of 0.3 Gm (5 grains) of nirvanol for children from 9 to 14 years, with a corresponding smaller quantity for children below this age—about 0.25 Gm (4 grains) from 6 to 9 years. J. D. Pilcher and H. J. Gerstenberger (Am J Dis Child 40 1239, 1930) administered nirvanol in doses of from 0.1 to 0.15 Gm (1½ to 2¼ grains) 3 times a day to a child with chorea up to 14 years of age. Schlesinger states that the *daily dose of nirvanol should not exceed 0.3 Gm (5 grains)*. However, in a very few instances C. F. T. East and E. R. Cullinan (Lancet 2 190 (July 26) 1930) have administered the drug in daily doses of 0.4 or 0.5 Gm (6 to 7½ grains), while occasionally a daily dose of 0.6 Gm (10 grains) of nirvanol was given to patients by Pilcher and Gerstenberger and also by W. M. Whitaker (Arch Dis Childhood 5 44 (Feb) 1930) to 13 or 14 year old children. The treatment is continued until a reaction or signs of toxicity appear, when the therapy is discontinued. This symptom complex which occurs following the administration of nirvanol is known as "*nirvanol disease*".

**"Nirvanol Disease."**—The *incubation* period of nirvanol disease usually ranges from 7 to 14 days. It is generally recommended that the medication should be discontinued if symptoms have not developed within 14 days after beginning treatment. According to Schlesinger (*loc cit.*), if the rash or pyrexia have not appeared by the twelfth day, it is useless and even dangerous to proceed with the treatment but Whitaker states that it is worth continuing for 15 to 20 days before stopping. One of Whitaker's patients was treated for 22 days before he developed

nirvanol sickness, which was complicated by diplopia. According to this author, it appears that those patients who react to the medication within 7 to 12 days have the most marked symptoms of sickness. As in the case of serum sickness when there has been a previous injection of serum, a previous treatment with nirvanol seems to shorten the incubation period. For example, Whitaker found that a single dose of nirvanol several weeks after the patient has recovered from nirvanol sickness will be followed by fever, rash and pulse rise within from 6 to 10 hours.

**Prodromal Period**—According to Whitaker, the approach of the reaction may be suspected by the appearance of drowsiness after 3 or 4 days of the drug therapy. Just before the onset of the reaction Schlesinger (*loc cit.*) and East and Cullinan (*loc cit.*) observed that the choreic manifestations and sometimes the symptoms of mental instability are exaggerated. *Fever* develops, the temperature, according to Pilcher and Gerstenberger rising gradually to a maximum of from 102.2° to 104° F. (39° to 40° C) a few days later, at which time the eruption appears. H. T. Ashby (Arch Dis Childhood 5 42 (Feb) 1930) found that some of the patients, especially those of the female sex, develop enuresis the evening before the appearance of the rash.

**Period of Eruption**—The 3 cardinal manifestations of nirvanol disease are: (1) Fever; (2) a quickened pulse rate, and (3) rash. However, it should be borne in mind that this triad does not always appear in its entirety. Thus, in a group of 15 cases treated by East and Cullinan (*loc cit.*), only 4 developed the entire symptom complex. In 3 of his patients the rash was present alone; in 1, fever, and once there was quicken-

ing of the pulse, the rash appearing without fever

The eruption or exanthem generally appears at the height of the fever, while usually morbilliform, may be scarlatiniform or urticarial. Pilcher and Gerstenberger (*loc cit*) According to East and Cullinan (*loc cit*), the rash usually appears first on the trunk, from whence it spreads to the face, trunk and back. H. Ashby (*loc cit*) states that the rash starts at the back of the hands or on the buttocks and spreads to the trunk.

Pressure points, especially the elbows and buttocks, are particularly affected. The macules are slightly raised and can be palpated and vary in intensity in different parts of the body. The lesions are bright red at first, according to East and Cullinan; later dusky in color. As the lesions progress they coalesce to a brilliant sheet of intense color which is most pronounced on the extensor surface of the limbs. An *enanthem* may be present, characterized by a flush of the buccal surface with the formation of tiny, dewy vesicles. Upon withdrawal of the drug, according to Pilcher and Gerstenberger, the rash fades, the cycle lasting about a week, or, in severe cases, even 2 weeks. Ashby states that the rash generally is faintly visible for 1 day, well developed for 2 days, and takes 1 day to fade and to completely disappear. East and Cullinan point out that desquamation does not occur.

According to Whitaker (*loc cit*), the patient may complain of *headache*, *burning of eyes*, occasionally *photophobia*, and *mild soreness* of the throat. There may be some itching of the skin. East and Cullinan note that drowsiness may be present. Ashby observed that some of the children lose the knee-jerks about the time the rash appears and do not regain them for a few days. While the

choreic movements and the mental manifestations may be aggravated during the attack of nirvanol disease, they usually subside with the rash, sometimes, according to Schlesinger (*loc cit*) with dramatic rapidity.

*Complications*.—The nature of the complications of nirvanol sickness, Pilcher and Gerstenberger believe, suggests that they are due to an unexplained idiosyncrasy, such as had been noted to follow the administration of small doses of acetylsalicylic acid, for instance, rather than to overdosage. The complications usually consist of irritation of the mucous membranes, *stomatitis*, *conjunctivitis*, *edema of the face*, and *urticaria*, and rarely, of *vulvovaginitis*, *balanitis* and *irritation of the urinary tract*, with *bloody urine*, in 1 case there was *exudation into the lungs* resembling pneumonia. *Diplopia* occurred in one of Whitaker's patients. K. Majerus, according to Whitaker, reported a fatal case of *acute hemorrhagic nephritis* due to nirvanol, occurring in a man suffering from a streptococcus empyema.

Two of the patients of East and Cullinan developed a marked degree of drowsiness, amounting practically to *coma*, while another patient developed a temporary *heart block*. Pilcher and Gerstenberger contend that complications have not proved serious in children, stating they have seen no reports of fatalities from the use of nirvanol as has been noted in adults.

*Relapse*.—Secondary reactions have occurred several days after the sickness with a return of the rash and fever, according to Whitaker. Keller suggested that reactions of the type were due to exposure to sunlight. Experimentally, Whitaker was not able to produce a return of symptoms by exposing 2 of his patients to sunlight.

*Blood*—Certain changes occur in the blood as the temperature rises and the rash appears a diminution in the *leukocytes* with a relative *lymphocytosis* and an *eosinophilia* as high as 15 per cent, a monocytosis and thrombopenia may occur and are considered by B Leichtentritt, W Lengsfeld and M Silberberg (Med Klin 24 764 (May 18) 1928) as characteristic of nirvanol disease. According to Pilcher and Gerstenberger, all these changes may not occur in the same patient, nor at the same time in a given patient. The *eosinophilia* is considered to be the most constant sign, although it is to be borne in mind that eosinophilia is not an uncommon finding in chorea. According to Whitaker, eosinophilia sometimes seems to be the only sign of a reaction. It disappears and the count returns to normal within 2 weeks. Whitaker did not lay much stress on the constancy of the relative lymphocytosis. The polymorphonuclear cells were increased above the admission figure in 4 of his patients, decreased in 3, and virtually the same in 1.

In 6 of a group of 10 patients observed by Whitaker a slight leukopenia was present, in 3 the blood count was unchanged, while in 1 patient with a throat infection there was an increase in the total count.

H H Ray and J S Cunningham (Am J Dis Child 39 1205 (June) 1930) found that phenylethylhydantoin was more effective than other drugs in the treatment of chorea. The mean duration of chorea from beginning was 31 days when nirvanol was used and 115 days when other drugs were administered. The majority of Whitaker's patients showed either marked improvement or a complete absence of active chorea within the first week of the re-

action. In all cases there was no active chorea after 1 month. Schlesinger, too, observed that as the rash subsided the symptoms often subsided with dramatic rapidity, generally disappearing entirely within a week or 10 days.

The most dramatic improvement is obtained in the severest and most acute cases of chorea, although Schlesinger has obtained some successful results with the drug in long-standing choreic cases, where other therapeutic measures had failed. Ray and Cunningham also state that mild chorea is not so rapidly cured as the severe form. However, Schlesinger observed that improvement bears no relation to the stage of the acute chorea at which the treatment is begun.

The exact *mechanism* by which the therapeutic results are obtained, still seems to be a puzzle. Whitaker states that patients improve whether the marked signs of sickness, such as fever and rash, are present or not. East and Cullinan state that the reaction is not necessary for improvement. Pilcher and Gerstenberger report that most observers seem to agree that the drug is most beneficial in severe cases of chorea in which a sharp febrile reaction follows its use. Whitaker, too, states that those cases having the most severe reactions do certainly show the most marked and rapid improvement. This author further points out that there is no evidence to support the idea that a sudden shift in the acid-base balance is induced at the time of the reaction.

Since the drug is capable of producing alarming symptoms, Whitaker as well as Pilcher and Gerstenberger contend that its use should probably be limited to hospital practice. The patient during the treatment should be confined to bed. Because of the possible danger of in-

juring the bone-marrow leading to an aleukemia, similar to that produced experimentally in laboratory animals (see Supplement to Sajous's Analytic Encyclopedia of Practical Medicine, 10th Edit, Vol. X, p 213, 1930) Ray and Cunningham recommend that frequent blood counts be made in all patients treated with nirvanol. However, Pilcher and Gerstenberger could find no report of injury of this type following the treatment of chorea with the drug. Although the symptoms are improved and the attack of chorea is cut short in many cases in quite a striking manner, the question, as East and Cullinan see it, is whether it is right to use a drug which can produce so variable and uncertain a reaction to treat a disease which is said to be self-limited. The main justification would rest upon the demonstration that the abolition of chorea prevented the carditis. Ashby, for example, states that with the use of nirvanol, the chorea is checked before rheumatic infection does harm to the heart. However, it is not yet proved that the rheumatic infection is abolished, in fact, 2 patients observed by East and Cullinan developed rheumatic fever shortly after a nirvanol reaction. These authors believe that the use of nirvanol should be restricted to cases which show no signs of improvement after 4 or 5 weeks' treatment along ordinary lines.

**Fever Treatment of Chorea.**—According to G Hétenyi (J. A. M. A. 97: 1556 (Nov 21) 1931) fever treatment of chorea, induced by milk injection, was recommended by Kern in 1923. It is still a question as to just how much of the beneficial effects obtained with the administration of nirvanol is due to the febrile reaction produced by the medication or how much is the result of any specific effects of the drug itself.

**Relapsing Fever.**—Knowing that recurrent infections may modify the course of chorea or even arrest the progress, I Mas de Ayala (An de Fac de med Montevideo, 15 544, 1930, J A M A 96 227 (Jan 17) 1931) produced experimental relapsing fever with the *Treponema hispanicum* in a 12-year-old boy with chorea, who had failed to respond to all previous treatments. The chorea had become progressively worse for 2 years. The fever treatment comprised 4 febrile attacks, after the fourth attack the patient began to improve. Total and permanent recovery was secured after the fourth attack.

**Typhoid; Paratyphoid Vaccine Therapy.**—Lucy P Sutton (J. A. M. A. 97 299 (Aug 1) 1931) treated 24 cases of chorea with intravenous injections of typhoid-paratyphoid vaccine as a means of producing fever. The first dose of vaccine usually ranged between 0.2 and 0.25 c c. This has always produced a sharp febrile reaction, in 1 case, 107° F (41.6° C). It is probably wiser to give even a smaller initial dose (0.1 c c) to determine the individual's reaction to the treatment. Succeeding doses are determined by the reaction to the first dose, i.e., if the temperature has risen to 105° or 106° F (40.5° or 41.1° C) with the first dose, the same amount is given the next day. Usually a third dose of the same amount does not produce much fever. As much as 2.5 c c has been given at a time but not as a first dose.

The reaction begins about 20 minutes after the injection; there is a chill, the child becomes quite uncomfortable, and choreiform movements are increased. The temperature then starts to rise and reaches the peak in from 2 to 4 hours, remaining at this point for about an



hour The whole reaction is over and the temperature back to normal usually in from 6 to 8 hours If the temperature reaches  $106^{\circ}\text{F}$  ( $41.1^{\circ}\text{C}$ ) **acetylsalicylic acid**, 5 grains (0.3 Gm) is given and an **ice-bag** applied to the head Occasionally the temperature is elevated the next day to about  $102^{\circ}\text{F}$  ( $38.9^{\circ}\text{C}$ ), when this occurs either no injection is given that day or the last dose is repeated

The progress of the chorea has been used as a guide to the continuation of the treatment Most cases have appeared to need a febrile period of about a week, others need more The results thus far have been good There has been prompt cessation of the symptoms, and the course of the disease in these patients has seemed to be greatly shortened In the cases reported, the average duration after treatment was started was from 8 to 9 days

**Magnesium Sulphate.**—G Marinnesco, O Sager and G T Dimischiotu (Ann de méd 27:237 (Mar) 1930) treated 5 cases of chorea with favorable results by subarachnoidal injections of magnesium sulphate (0.008 mg— $\frac{1}{8000}$  grain—per kilogram— $2\frac{1}{2}$  pounds—of body weight in 25 per cent solution) within from 5- to 6-day intervals

**Sodium Salicylate.**—L Aydillo (Arch de neurobiol 9:69 (Jan-Mar) 1929), Am J. Dis Child 39:879 (Apr) 1930) used intravenous injections of sodium salicylate and claimed great success in the treatment of chorea Ten cc ( $2\frac{1}{2}$  drams) of the solution (sodium salicylate, 10 Gm— $2\frac{1}{2}$  drams—pure dextrose, 5 Gm— $1\frac{1}{4}$  drams—sterile distilled water, 100 c.c— $3\frac{1}{2}$  ounces) were injected every 2 days until complete recovery was obtained The latter was effected in 6 cases with less than 20 injections. In 2 other patients,

1 showed complete recovery before the twentieth injection, while the other was practically cured after 30 injections

C B Leech (J A M A 95:932 (Sept 27) 1930) gave daily rations of 20 grains (1.3 Gm) of acetylsalicylic acid for a 6-month period to 67 children with potential heart disease and inactive rheumatic heart disease A control group consisted of 79 children with similar potential and acquired rheumatic heart lesions Fewer recurrences of chorea occurred in the experimental than in the control group. The control group did not do so well as the experimental series in the matter of gain in body weight, improvement in heart rate, general body comfort and functional classification based on ability to carry on normal activity without discomfort There was no evidence of any effect of the drug on the slowly progressive development of mitral stenosis

**Parathyroid Extract.**—R G Tuck (*loc cit*) tried Fowler's solution, diet, rest, absence from school, and the like, in the treatment of chorea with little beneficial effect when the results were summed up The author's experience with parathyroid extract alone was far from being satisfactory However, upon administering both **parathyroid extract** and **Fowler's solution** rather striking beneficial results were obtained He administered from 5 to 8 drops (0.325 to 0.5 cc) of Fowler's solution, 3 times a day, and 3 injections of  $\frac{1}{10}$  grain (0.006 Gm.) of parathyroid extract at weekly intervals.

**Calcium.**—In this disease calcium has also been found useful Calcium lactate, according to Stephens (*loc cit.*), given with parathyroid extract tends to lower the "basic blood-pressure", as the latter falls, the other signs and symptoms diminish

**CILIARY BODY. — HEMANGIOMA.**—R K Daily (Am J Ophth 14 653 (July) 1931) reports the case of a 5-months old child who was brought to him with photophobia, lacrimation and bulbar congestion. Examination revealed increased tension, and when the blood in the anterior chamber had become absorbed, a dark brown growth was observed in the angle. A diagnosis of recurrent hemorrhages due to an intraocular growth was made and enucleation performed. Histological section showed a capillary hemangioma of the ciliary body.

**CINCHOPHEN.**—J B Ross (Canad M A J 24 632 (May) 1931), quoting Rabinowitz, gives a list of the various preparations in which cinchophen is found, which follows.

Phenyl-cinchonic acid, Atophan, Novatophan, Atophanyl, Dinodoatophan, Biloptin, Oxyliodide; Quinophen, Agotan, Neo-cinchophen, Quenophan, Leucotropin, Atophanurotropin, Fantan, Iriphan, Tolysin, Weldon, Farastan, Atouquinol.

**POISONING.**—During the past 2 years a great many cases of cinchophen poisoning have been recorded in the literature. J B. Ross (Canad M A J 24.632 (May) 1931) reports 5 cases, 3 of which resulted in death. Autopsies on these cases showed marked liver damage with a small shrunken liver and extensive cytolysis, in all appearances similar to that seen in acute yellow atrophy. In each case the patient gave a history of having taken some drug containing cinchophen, but neither the period of time nor the dosage showed any relation to the degree of disease present. In 2 of the 3 cases which died, operation had been performed, in one case for gall-bladder disease and in the other to ankylose a diseased hip. Ross

concluded that any anesthetic, operative shock or period of starvation, with depletion of the glycogen stores of the liver, might cause an acute cytolytic collapse of the cinchophen poisoned liver. This substantiated the findings of M A Rabinowitz (J A M A 95 1228 (Oct 25) 1930).

Two additional cases are reported by E Vajda (Med Klin 26 1404 (Sept 19) 1930), in which gastrointestinal upset and icterus followed the use of cinchophen derivatives. N Liedberg (Hygiea 91 801 (Dec 15) 1929), in reviewing the literature, found 29 cases reported and added 2 of his own. Of these 31 cases, 11 died and at autopsy 6 showed the typical liver changes seen in acute yellow atrophy. It is interesting to note that in 5 cases of this series of 31 cases, the cinchophen was given in dye for gall-bladder x-ray work and not as a therapeutic agent.

L Parsons and W G Harding, Jr. (Am J M Sc 181.115 (Jan) 1931) collected 15 cases of fatal cinchophen poisoning in the United States. In each case pathological changes in the liver were found and were studied at autopsy. They concluded that intensive dosage with cinchophen is apt to produce an acute hepatic degeneration. However, they also feel that cinchophen derivatives given in moderate doses, if continued for a long period of time, may give rise to either a subacute or chronic hepatic disease.

D. C Beaver and H. E. Robertson (Am. J. Path. 7 237 (May) 1931) reported 5 fatal cases of cinchophen poisoning treated at The Mayo Clinic following cinchophen therapy elsewhere. They also concluded that cinchophen poisoning is chiefly shown as a degeneration of the parenchymatous tissue of the liver and believe this to be patho-

genically related to toxic cirrhosis. They believe that unknown factors are significant in creating an idiosyncrasy for the drug and that dosage is not the vital factor concerned.

In studying cinchophen poisoning from a pharmacological standpoint, K. Eimer (Deutsche med. Wchnschr. 57:1653 (Sept. 25) 1931) came to the conclusion that the toxic effects were the result of cumulation of the drug in the patient's tissues and he suggested as treatment the administration of dextrose and insulin and stimulation of bile flow by means of duodenal drainage and various cholagogues, such as magnesium sulphate. In his case, the patient recovered. Eimer believes that in cinchophen therapy, drug-free intervals should be carefully adhered to.

L. J. Stacy and F. R. Vanzant (Minnesota Med. 13:327 (May) 1930) report the case of a woman who had taken large doses of cinchophen over a considerable period of time and developed all the symptoms of an acute yellow atrophy with jaundice, etc. They tried a treatment of a high carbohydrate diet or oral administration of calcium lactate in large doses, calcium chloride, and intravenous glucose, both with and without insulin. The case terminated in death and at autopsy the liver showed the typical gross and microscopic picture of acute yellow atrophy.

**COLON.—FUNCTIONAL DISORDERS.**—Some major or minor disorder of the colon was noted on clinical, fecal, or radiologic evidence in 2086 out of 4000 cases reported by E. I. Spriggs (Quart. J. Med. 24:533 (July) 1931). The list includes all patients with symptoms referable to the colon, except those with simple delay only, and those whose condition made

complete study impossible. Of this number, a group of 242 cases having functional colonic disorders as the chief finding was selected for study. There are included 157 cases of *mucoous colitis* and 85 cases of *irritable colon*, *spasm* and *nervous diarrhea*.

**ETIOLOGY.**—The causes of functional disorders of the colon are numerous. Infections either of the bowel itself, as in acute diarrhea, dysentery, or from distant foci, or in association with achlorhydria, or secondary to disease of the gall-bladder, appendix or other organs, are mentioned by Spriggs as possible etiologic factors. Parasites may also be of importance. Poor hygiene including exposure, too much smoking, bad water, ice-water, and bad food are other causes mentioned. However, the 2 main causes, according to nearly all observers, are *neurosis* and *constipation*. Regarding the latter condition, Spriggs believes that the treatment for real or alleged constipation, *viz.*, that by irritating aperients, is as potent and frequent a cause of colonic disorder as constipation itself. In the present series of 242 cases, there were 47 with diarrhea who took no aperient, of the remainder, there were only 18 who took no aperient, and 50 whose history was uncertain. Of the remainder, 70 took a purge daily.

It is the impression of Spriggs, therefore, that moderate constipation is less harmful to the colon than the treatment of it by irritative aperients. These interfere with the rhythm of the bowel, setting up inhibitions and spasms, causing first a too rapid passage and later local stasis, they render the feces more fluid than they should be and thus favor abnormal bacterial and putrefactive growth. Among irritative aperients, besides calomel and the drastic vegetable

purgatives, are included the vegetable laxatives such as rhubarb, cascara, and senna, which contain a certain chemical irritant, one of the anthracene bodies. He includes also the regular use of salines.

The average age of this series was 44 years for men and 42 years for women. Inherited constitutional weakness is suggested by a family history of cancer in 18 per cent, tuberculosis in 12 per cent, and neurosis in 9 per cent. The lack of occupation of many of these patients is obvious, and Spriggs considers that work would cure some and prevent the illness of many.

**PATHOLOGY.**—Whether the nervous factor is primary or not, there is a local neuromuscular disturbance which may be reflex or due to irritation of the mucous membrane itself. The irritation may be bacterial or toxic. Spriggs (*loc cit*) suggests that the circulatory factors may be important. Lack of normal bowel motility results in venous stasis and poorer nutrition of the bowel, as well as increased fermentative and putrefactive activity in the lumen. The importance of autointoxication has been over-emphasized, according to Spriggs. For example, in 90 cases admitted with that diagnosis, 32 were found to be suffering from the following diseases: gastric and duodenal ulcer (8); diverticulosis (7), cholecystitis (6); syphilis (3); rectal growths (2), growth of the lung, nephritis, gout or heart disease, and in the remainder the main feature was neurasthenia.

Regarding bacteriologic study of the feces in these conditions the author considers that the repeated culture of the stool in these disorders is probably not worth the time and labor involved.

**SYMPTOMS AND SIGNS.**—In functional disorder of the colon the dis-

turbance may vary from little or none in many cases of simple constipation, to complete invalidism with much suffering in severe mucous colitis. In the cases discussed some kind of pain or discomfort was complained of by 80 per cent of the patients, ranging from an ache or dragging, or colicky pains, cramps, distention with gurgling, and flatulence to acute paroxysmal crises with vomiting. Pain and tenderness over the colon appeared in 55 per cent, epigastric pain was present in 26 per cent, frequently being related to food and simulating organic gastric disease. Nausea occurred in 24 per cent, and vomiting in 16 per cent. The chief nervous symptoms were weariness, depression and headache.

Physical examination frequently reveals the colon contracted into a hard cord. Gastric analysis in 111 cases of this series showed achlorhydria in 2 per cent, subacidity in 23 per cent, and hyperacidity in 41 per cent. Fecal analysis may reveal scybala with some mucus or semisolid movements with excessive mucus, or mucous casts in the mucomembranous types. Bowel motility by x-ray may be increased or decreased, usually the latter, according to Spriggs (*loc cit*). Changes in muscle tone were noted in 43 per cent of the 242 cases reported. Irregular haustrations were present in 29 per cent. Areas of atony were present in about one-third of the cases.

Of these 242 cases of functional disturbances of the colon reported by Spriggs, 50 per cent. had evidence of some other disorder of the alimentary system, either in the past or present. The most frequent associated lesions were appendicitis, gall-bladder disease, peptic ulcer, adhesions, parasitism, or duodenal diverticula. Coloptosis was

present in 12 per cent, as judged by the criteria of a low transverse colon and the hepatic flexure in the iliac fossa

**DIAGNOSIS.**—The following types of diseases enter into the problem of differential diagnosis, according to Spriggs (*loc cit*)

1 Those causing dyspepsia, such as gastritis, peptic ulcer, gall-stones, and appendicitis. The error is usually to suspect one of these lesions when the colon may be responsible

2 Dysentery, parasitism, diverticulosis and diverticulitis, and chronic obstruction (possibly cancer) must be excluded

3 Diseases arising from outside the colon which often simulate functional colon disorders are achylic and pancreatic diarrhea, appendicitis, Graves's disease, pelvic inflammatory disease, and sometimes renal colic

Even when the colon is known to be disordered and seems to be responsible for all the symptoms, a complete survey should always be made, according to Spriggs

**PROGNOSIS.**—In nearly all cases the colon and the patient recover if the constipation can be cured without use of chemical irritants. Even cases of mucous and mucomembranous colitis with neurasthenia may recover within 2 or 3 months with thorough and whole-time treatment, according to this authority

**PROPHYLAXIS.**—Spriggs points out the importance of hygienic measures such as **regular meals, exercise, and sleep, a plain mixed diet properly chewed, and the cultivation of a daily bowel movement, avoiding aperients other than fruits, plenty of water, and mineral oil if needed.** Daily movements are not imperative, but if con-

tinued delay occurs, active treatment should be instituted

**TREATMENT.**—Spriggs states that the main rules of treatment are to allay anxiety, to abolish laxatives and purgatives, to give a suitable diet, and to regulate rest and exercise. In severe cases a change of environment may be necessary

In regulating bowel habit this author suggests that an attempt to move the bowels be made at a regular time each day for a period of 10 minutes. If there is no result a **glycerin suppository** may be used. If no movement follows, the same routine is followed for another day. If still no movement, an **enema** should be given.

The diet need not be greatly restricted in most cases, according to Spriggs. Meat is best reduced, being replaced by eggs, fish and cream cheese. The amount of milk used depends on whether or not weight gain is desired. Fruits and green vegetables are advised by this author for each of the 3 meals. **Acidophilus** milk and lactose have given favorable results in his hands. **Massage of the abdomen** is sometimes valuable, especially in atonic colons without painful symptoms. **Regular exercise** is advised and some special **abdominal exercises** are used as indicated. **Colon irrigations**, if gently done, are of value in some cases. **Mental and physical rest** are imperative, the degree of the latter depending upon the seriousness of the disorder. **Focal infection** and other abnormalities must be treated.

In *spastic disorders* of the colon, some special measures are suggested by the author. **Tobacco** must frequently be given up entirely. **Rough foods** are **contraindicated**, excluding whole wheat bread, raw fruit, and salads. Of

the drugs, belladonna and hyoscyamus are the most useful, while intestinal antiseptics are sometimes advised. Aperients are rarely advisable. Normal saline enemas, or evening injections of warm olive oil to be retained, or oil and water enemas are the most suitable local injections according to Spriggs.

As to results of treatment, the following figures are given. 208 patients were treated, 1 per cent were worse, 9 per cent were not improved, 90 per cent improved greatly or were well while under treatment. These diseases do not kill, but they cause weakness and misery. The writer states that if the physician can learn more, and can educate the public in regard to the hygiene of the colon, a great addition will have been made to human health and happiness.

**COLITIS, IDIOPATHIC ULCERATIVE.—SYMPTOMS.**—During the period of acute general symptomatology in ulcerative colitis, J Felsen (Arch Int Med 48:786 (Nov) 1931) states there is usually acute inflammation of the mucosa of the colon. Spreading of the ulcers, or their confluence, may be unindicated by increase in general symptoms. A single remaining ulcer may cause persistence of diarrhea, with or without blood, pus, and mucus, whereas ulcers may persist in abundance long after the diarrhea and all other symptoms have subsided.

The onset of an intramural abscess is heralded by sudden persistent pain accompanied by fever. The abscess usually occurs in a solitary follicle, it tends to evacuate into the lumen of the bowel, rather than to penetrate the 2 thick muscular layers of the gut.

**DIAGNOSIS.**—According to Felsen, clinically, there is a diarrhea of varying severity, with passage of mucus, blood

and pus, colic and tenesmus. By direct inspection, *via* the sigmoidoscope, there is seen hyperemia of the mucosa of the colon, in which are scattered abscesses and ulcers in various stages of healing, blood and pus. The ulcers may tend to run together, indicating tunneling, with an overlying granular mucosa between them. In healing or healed cases fibrosis of the intestinal wall with stricture or diffuse contracture of the lumen may be seen.

Laboratory findings are absence of *B typhosus*, *B paratyphosus A* and *B*, and *B dysenteriae* by culture, and of *B tuberculosis* by smear, ova and parasites and their encysted forms. Serologic studies should show negative Wassermann; nonagglutination of *B typhosus*, *B paratyphosus A* and *B*, *B dysenteriae* and *B paradysenteriae of Costellam*, 9 strains of the last mentioned organism should be tested with the patient's serum diluted 1:80.

The intestinal flora of ulcerative colitis differs quantitatively from the normal, rather than qualitatively, *e g*, in some cases of ulcerative colitis a type of streptococci are found in almost pure culture, whereas they normally constitute only a very small proportion of the bacterial content. In one case cultures taken almost daily showed pure enterococcus, with absence of *B coli*, over a period of 2 months.

Clinical observations indicate that there is a mild type of ulcerative colitis which tends to terminate spontaneously; also patients with acute ulcerative colitis sometimes improve and become symptom-free while the ulcers persist. Recurrence is frequent and usually takes place within 3 years.

**TREATMENT.**—There are 3 valuable methods of treatment, *i e*, oxygen, bacterial vaccine, and irrigation. The



first two, used concurrently or separately, brought about improvement, or possibly cure, in 90 to 100 per cent of 60 cases, with only 1 death, which occurred in a patient treated with oxygen alone. Irrigation, however, gave improvement, or possibly cure, in only 63 per cent of 41 cases, with about 15 per cent of deaths.

The average duration of the disease in these various groups was from 7 to 11 months. Sixteen cases were used as controls, of which 10 were untreated, and 20 per cent died, 3 were given colonic inflations of carbon dioxide and 3 of nitrogen, all 6 showing no mortality, but no improvement or cures.

**Method of Oxygen Administration.**—The oxygen is run through an indicator bottle holding water at about 40° C (104° F). This precaution is unnecessary in warm weather. Through an ordinary hard rubber enema tip or soft rubber catheter, 250 c c of oxygen is introduced into the rectum, during alternate hours, until 7 hours' flow have been administered. Twenty bubbles per minute supplies the desired 250 c c of oxygen per hour. The oxygen is gradually absorbed. It moderately distends the intestines up to the pylorus, but has not been demonstrated to enter the stomach.

The oxygenation seems to diminish or eliminate spore-bearing anaerobes, and encourages the growth of aerobes.

No intramural abscesses have occurred after the oxygen treatment was well under way.

The *B. welchii* type of spore bearing anaerobes disappear promptly.

**Vaccine Treatment.**—Vaccine treatment is especially useful in ulcerative colitis if the intestinal flora is predominately streptococcic. The type is usually that of Huntoon and McElroy

or the organism of Barger. The use of vaccines is believed by Felsen to aid in preventing such complications as arthritis, myocarditis and renal infections, which frequently cause death of the patient after he is more or less recovered from his colonic lesions.

**X-RAY EXAMINATION OF COLON.**—In a discussion of the technique, tactics and results of the x-ray examination of the colon, H. H. Berg (Röntgenpraxis 3: 145 (Feb 15) 1931) states that a film of the entire abdomen, before the administration of the contrast medium, may sometimes reveal evidence of obstruction through abnormal gas collections. The author mentions the observation of the passage of the barium meal because of its value in a study of motility and function, but the barium enema method replaces the oral administration method when morphologic changes are to be shown. The colon must be entirely empty when the barium enema is administered, as retained fecal material may lead to errors. The capacity of the colon is variable and no set quantity of opaque medium can be considered as correct. Certain cathartics and irritating or cold enemas may result in a decreased capacity through irritation. In *colitis*, capacity may be decreased or increased. Too large a quantity of the opaque medium interferes with a study of the mucosa of the colon. In many cases it is advisable to use a small quantity of opaque medium combined with inflation by air (Fischer). The study of the mucosa itself is undertaken after the colon is evacuated. Complete emptying speaks for colitis (Hickey has advocated emptying the colon by catheter under fluoroscopic observation and claims that this method results in a superior demonstration of the function of the colon).

It is often necessary to repeat the examination, using Fischer's method of air inflation, after the routine barium enema examination has been completed. Reliance upon fluoroscopy alone is dangerous. The Potter-Bucky diaphragm is of great value when large areas are included on one film.

The roentgenologist must have a free hand in the conduct of the examination and should take the history of the patient into consideration. He should outline the procedure and the decision as to the necessity for re-examination should be his responsibility. Failure to diagnose cases of *carcinoma of the colon* is generally due to faulty methods (for example the ordering of a barium meal and failure to return the patient for a barium enema after the barium meal examination has been completed).

Changes in the position of the colon without manifest disturbances of motility, are of no importance. The diagnosis of ptosis should not be made. Adhesions which do not interfere with motility are often of no clinical importance. The direct x-ray signs of disease of the colon are much more important than the functional disturbances. In other words, *the barium enema examination is much more important than the examination with the barium meal*.

**SURGERY OF COLON.—PROPHYLAXIS AGAINST PERITONITIS.**—Studies by F. W. Rankin and J. A. Bagen (Arch. Surg. 22:98 (Jan.) 1931) emphasize the value of *preoperative protection by vaccine* against peritonitis in procedures in which resection of parts of the large intestine are involved. It has been amply demonstrated that protection against lethal peritonitis can be established in animals. The relatively transient nature of such immunity is noteworthy. The

time element between vaccination and operation is important. The amount of vaccine injected has less significance but is important. The systemic reaction of the patient is often moderately severe but endures only a short period and is never alarming. That the logical preventive reagent is a vaccine prepared from streptococci and colon bacilli is suggested by the predominant presence of these organisms in the exudate in fatal cases of peritonitis and their vast predominance in and around malignant lesions of the large intestine.

The authors report a series of 222 cases in which vaccine was given, with 11 deaths from peritonitis; and a series of 58 cases in which vaccine was not given, with 13 deaths from peritonitis. Included in both series were all types of operations commonly performed on the colon at The Mayo Clinic.

**CANCER.**—J. Charrrier and R. Leibovici (J. de chir. 37:1 (Jan.) 1931) report 2 cases of cancer of the colon *complicated by a large abscess* surrounding the tumor and discuss 17 similar cases, which they have found in the literature. From this study they draw the following conclusions: A cancer of the colon complicated by a large abscess surrounding the tumor is not necessarily an inextirpable cancer. The suppuration may be a complication as early and revelatory as acute occlusion. A colonic cancer is an infected cancer, which can soon cause the development of an abscess in the peritoneum, in the retroperitoneal tissue or in the mesocolon. During the period of suppuration it is impossible to judge of the extent and operability of the cancer because the abscess increases tenfold the adhesions and the volume of the tumor. When the abscess has been drained and the colon put in a state of repose for a few

weeks, it is wise to verify again the condition of the primary neoplasm, in many cases a secondary exeresis will then be possible

With an abscessed cancer of the colon 3 methods are possible, according to whether the resection is immediate, early or delayed. Immediate resection is not to be recommended, since operation with the inflammation at its height is dangerous and requires the removal of a greater amount of the tissues than the actual volume of the tumor justifies. Early resection, after several days of exteriorization, is possible with the sigmoid colon when the abscess is not too large and when the tumor can be brought outside without the extensive separation of adhesions. The method of choice, however, is **delayed resection**. The first step is to **drain** the abscess and establish a **cecal anus**. This derivation puts the colon in a state of repose and often permits the complete cicatrization of the abscess in a few weeks, sometimes a fistula remains. Two or 3 months later, when the patient has somewhat recuperated and the inflammation has been reduced, a second intervention may be made to **remove the cancer**.

**DIVERTICULUM.**—According to W J Mayo (Ann Surg 92 739 (Oct) 1930), diverticula of the colon may be true or acquired. The former, whether congenital, traction or pulsion, contain all the intestinal coats in the sac, in the latter the intestinal mucous membrane pouches through small openings in the musculature, such as holes for vessels, or at muscle defects. The latter type often contains small hardened fecal masses. The sigmoid is nearly always involved in diverticulosis. If the entire colon is affected there is usually a gradual increase in the fre-

quency of the diverticula from right to left. Diagnosis is evident on x-ray examination.

Of 31,838 examinations of the colon made at The Mayo Clinic, 1819, or 5.71 per cent showed diverticula. Only 20 of these were less than 40 years of age. In 2139 recorded cases of diverticulosis, active diverticulitis were present in 696, 64 per cent of the patients were men. Obesity is not an etiological factor, nor is constipation. Inflammation is usually limited to one of several diverticula. A considerable length of bowel may be obstructed by edema and adhesive inflammation. Thus, in acute cases a tumor is usually present in the left lower quadrant. Group I includes self-limiting diverticulitis and peridiverticulitis, causing pain in the region of the mass, a moderate fever and gaseous distention. These patients are ambulatory in a few days and the mass disappears in a few weeks. Group II includes the cases with abscess formation and the development of a fistula and require surgical interference. Group III includes the cases showing obstructive symptoms. This may be due to hyperplasia, adhesions or angulation. In Group IV are the cases of carcinoma developing on a diverticulum. Carcinomatous change may be suspected when the tumefaction does not wholly subside, but remains as a chronic mass, causing more or less marked symptoms. The relation between carcinoma and diverticulitis remains conjectural. The distinction can usually be demonstrated by x-rays.

**Treatment.**—In acute cases **treatment** should be **tentative**. If an **abscess** forms it should be **evacuated**, to prevent the formation of a fistula. In **acute obstruction** **colostomy** should be done as close to the obstructed point as convenient. Subsequently the stenosis

ing portion plus the colostomy should be excised simultaneously. **Cecostomy** may be done instead of colostomy. The relief of *internal fistulae* is a serious problem, but **excision** of the fistula with repair of the sigmoid has been performed with good results.

**MEGACOLON (HIRSCHSPRUNG'S DISEASE).—Treatment.**—D E Robertson (Canad M. A J 24 359 (Mar) 1931) reports 6 cases of congenital megacolon or Hirschsprung's disease, which were treated by **operation on the lumbar sympathetic trunk**. The author gives detailed reports on 3 of these cases. In all of the cases cure was obtained. He believes that the lumbar sympathetic cord is approached most safely and easily by the extraperitoneal route.

F W Rankin and J R Learmonth (Ann Surg 92 710 (Oct) 1930) discuss the pathological anatomy of Hirschsprung's disease and certain types of constipation, and are of the opinion that neuromuscular dysfunction is the most probable cause in a large number of cases. The authors applied **section of the sympathetic nerves** of the distal part of the colon and rectum to a case of obstipation in which the cause of the difficulty was lack of rectal tonus.

The authors point out that the post-operative course of patients suffering from Hirschsprung's disease will be different from that of patients suffering from rectal constipation. More immediate benefit is to be expected in the former. The explanation for this lies in the fact that after operation the hypertrophied musculature of the colon is immediately available for effective peristalsis. In cases of rectal constipation, not only is hypertrophy of the muscular coat of the bowel absent, but also the long continued distention of the rectum

leads to atony and even atrophy of the musculature.

**CONJUNCTIVA.—CALCIUM EXCRETION.**—S Sanyal (Am J Ophth 14 1044 (Oct) 1931) reports a case of a girl, age 12 years, who complained of the secretion of sandy matter from her eyes which, on chemical examination, was found to be calcium urate. Sanyal considers this a case of faulty protein and calcium metabolism. The patient was accordingly given **cod-liver oil**, placed on a milk and **vegetable diet** and a prescription containing **calcium and thyroid and parathyroid extracts**. Improvement and cure followed within 2 months.

**PEMPHIGUS.**—Pemphigus is a rare disease attacking patients of all ages and sexes, and is not hereditary, according to W O Martin, Jr (Arch Ophth 33 744 (June) 1930). Its etiology is obscure and the subjective symptoms consist of soreness, tenderness, burning, and itching with diffuse discharge. The conjunctiva shrinks and symblepharon forms. By extension the cornea is involved and ulceration and suppurative keratitis ensue. Treatment is symptomatic.

**TUMORS.**—A case of *malignant melanotic tumor* in the tarsal conjunctiva is reported by O Hemonen (Finska lak-sällsk handl 72:261 (Apr) 1930) in which extirpation was followed by several recurrences. Microscopic examination of one of the recurrent tumors indicated changes of an epithelial nature, and the cells markedly resembled the tumor cells of the primary tumor.

*Plasmoma* begins as a small growth of the fornix spreading over the conjunctiva, and is not a tumor but a tissue reaction due to chronic irritation. Early and complete **excision** of the growth

followed by radium is the treatment recommended by P S Soudakoff (China M J 44 195 (Mar) 1930), who records 17 cases

### CONJUNCTIVITIS.—ACUTE AND CHRONIC.—*Treatment.*—

Birnbaum (Le Scalpel 369 (Apr 6) 1929) advocates a preparation of **diacetyl tannin** and **silver albuminate** for use in *acute* and *chronic conjunctivitis*. It is astringent and bactericidal.

**FOLLICULAR.—*Etiology.***—K Lindner (Arch f Ophth 122 391, 1929) states that he has no doubt that Noguchi cultivated the bacterium *granulosis* from mixed cases of trachoma and follicular conjunctivitis, and that this bacterium is not the cause of trachoma but one of the causes of follicular conjunctivitis.

***Treatment.***—Freezing by ethyl chloride has been found by L Collin (Monde méd 37 470 (Apr 1) 1927) to be an effective method of treatment for follicular conjunctivitis. The upper eyelid is everted, and while the cornea is protected the palpebral conjunctiva is quickly sprayed with ethyl chloride until freezing occurs. In recent and mild cases 1 treatment suffices. As a result of the treatment the granulations discharge their contents and are transformed into cicatricial tissue. Of 26 cases, mostly in school children, 20 were cured, 3 greatly improved, 2 improved, and 1 only slightly improved. Of 32 other cases in older patients, comprising mostly long-standing and complicated trachomas, 10 were cured, 12 greatly improved, 5 improved, and 5 slightly improved.

### GRANULAR (TRACHOMA).—

***Etiology.***—From their experiments with rats, A I Kendall and S R Gifford (Arch Ophth 4 322 (Sept)

1930) conclude that a lack of *vitamin A* is not essential for trachoma infection, but they do not disprove the theory that it may be a contributory cause.

In a bacteriological study of trachoma W C Finnoff and P Thygeson (Arch Ophth 5 527 (Apr) 1931) recovered from 5 of 13 white persons, 1 Japanese and 2 of 14 trachomatous Indian children, a minute Gram-negative motile rod apparently identical with that described by Noguchi under the name "*bacterium granulosis*". Inclusion bodies and initial bodies are usually absent in advanced trachoma, but bacteria morphologically identical with *B granulosis* were found on and in the epithelial cells in smears taken from trachomatous patients and from animals having the experimental disease. These bacteria are, therefore, considered more characteristic of trachoma.

Inoculation of monkeys with suspensions of *bacterium granulosis* produced granular conjunctivitis identical with that described by Noguchi and also with that which resulted from the injection of human trachomatous material. In 1 of 2 monkeys exposed, infection by contact occurred.

The results of their studies seem to confirm those of Noguchi in all essential respects. Because trachoma in monkeys is not identical with trachoma in human beings, it may be necessary to inoculate human beings in order to determine more conclusively the etiologic relationship of *bacterium granulosis* to trachoma.

E B Tilden and J R Tyler (J. Exper Med 52:617 (Oct) 1930) isolated 6 additional strains of *bacterium granulosis* from cases of trachoma occurring in the Indian schools of Arizona. They suggest that the bactericidal effect which cocaine has on the organism

may explain the negative results of cultivation experiments reported by other workers

H A Reimann and A Pillat (J Exper Med 53 687 (May) 1931) suggest that trachoma is in most instances a double infection (1) a superficial conjunctival infection, associated with inclusion bodies, (2) a deep infection of the subepithelial layers probably caused by the *granulosis bacillus* P K Olitsky, R E Knutti and J R Tyler (J Exper Med 53 753 (May) 1931) formed the opinion that the florid type of trachoma might possibly be due to secondary infection which converts a follicular conjunctivitis into a more severe destructive lesion of the hyperemic granulopapillary type

Typical *inclusion bodies*, identical in morphology and staining reaction with those found in trachoma and "inclusion-blennorrhoea," were obtained by S R Gifford and H K Lazar (Arch Ophth 4 468 (Oct) 1930) in material from artificially induced inflammation of the conjunctiva. They used chemical irritants and organisms from sources entirely independent of trachoma or inclusion blennorrhoeas to induce conjunctivitis. They consider that the presence or absence of inclusion bodies is of no importance in the etiology or diagnosis of trachoma

O Aust (Arch. f Ophth 123 93, 1929) reviews 17 cases of conjunctivitis in which *inclusion bodies* were found. They were all acute granular conjunctivitis, without scarring. He believes that this form of acute conjunctivitis or acute trachoma in which inclusion bodies are present is always derived from a genital source and never cicatrizes.

**VERNAL.**—In summarizing the literature on vernal conjunctivitis M W Jacobs (Am J Ophth 14:640 (July)

1931) states that endocrinology, the sympathetic nervous system, allergy and photosensitivity have been considered etiological factors. Radium is considered one of the best means to relieve the discomfort in this disease. Cassimatis recommends *autohemotherapy*. Tot-scheff uses *lactic acid*.

**CONSTIPATION.—ETIOLOGY.**—J V Fildian (Brit M J 2 1080 (Dec 12) 1931) commends the modern view of constipation, which has, unfortunately, been contributed to by Hurst and Alvarez. He says "the haggard faces and emaciated frames of Arbuthnot Lane's 'kinks' are now recognized as the stigmata of chronic cascara poisoning, and we spend our days combating the precepts of our medical forbears, and in persuading people to leave their harassed bowels alone"

The gastrocolic reflex, a mass peristalsis in the colon produced by entry of food into the stomach, was first described by Hurst. It is a remarkable phenomenon of the colon, and is different from any of the movements of other parts of the alimentary tract. This mass peristalsis produces sudden transference of large blocks of the contents of the colon from one part of the colon to the succeeding part, or even from the proximal end of the colon to the distal end. It occurs only 3 or 4 times a day, and has never been seen, by the naked eye, in man. It was first observed radioscopically by Holznacht, and later studied by Hurst and by Barclay, but its exact mechanism is still incompletely understood. It appears, however, that when the longitudinal muscles of the colon begin to contract, the proximal end of the colon, closed by the ileocecal valve and sphincter, acts like the piston



of a syringe, propelling part of the contents of the ascending colon around the hepatic flexure into the transverse colon. The hepatic flexure has a valve-like function, breaking the column of feces and preventing the projected contents from slipping back when the subsequent relaxation occurs.

Defecation is the natural result of the occurrence of mass movement in the distal half of the colon. It is modified by necessity, imposed by civilized conditions of life, which abolishes the rectal reflex, resulting in stretching of the rectum, so that it accommodates the feces until voluntary defecation occurs. This abolition of the involuntary rectal reflex is called *dyschezia*.

Fiddian considers Hurst's division of constipation into the 2 conditions, *ie*, dyschezia and colonic stasis, as a great contribution to the knowledge on the subject. Hurst found that the rectal reflex is produced by sudden increase of pressure in the rectum, normally produced by the entry of fecal matter from the distal colon. Slight inflation of a balloon in the rectum produces an active rectal reflex, if the pressure so produced is allowed to remain constant, it ceases to produce the reflex in a short while, and a further inflation is necessary to produce it again. The rectum can be made to tolerate enormously greater pressure than that which originally produced the reflex, by successive increases in the inflation of the balloon. The same process occurs in dyschezia. The rectum becomes less and less excitable, until it becomes a receptacle from the colon, as does the urinary bladder for the kidneys.

Fiddian believes that, in the present state of evolution, the evacuation of the rectum is not under voluntary control. [The editor disagrees with this opinion,

and believes that a relatively normal person can voluntarily produce the rectal contractions necessary to provoke the rectal reflex, if rectal contents are present, and that simply sitting at stool, without conscious effort, tends to have the same effect. The editor believes that "habit time" could not be formed if one of these factors was not capable of provoking the reflexes which produce defecation.]

All civilized human beings have some degree of dyschezia. It is necessary, and not incompatible with perfect health. It may cause anal fissure and hemorrhoids, but the feces are practically detoxicated by the time they reach the rectum, and what toxins remain do not seem to be absorbed therefrom.

According to Fiddian (*loc cit*), dyschezia is the trouble with the vast majority of patients who complain of constipation, and this should be treated by the periodical simple enema, for when a purgative is given to a dyschezic, all the gastrointestinal movements are accelerated until the sluggish rectal reflex is excited by rapid additions to the rectal contents. Thus, the entire complex process of digestion and absorption is disordered in order to stimulate the rectal reflex.

The contents of the terminal portion of the small intestine are highly toxic. Practically all the useful products of digestion have been absorbed and the residue contains much bacterial and chemical poison. Normally, detoxication of this material is achieved in the cecum and ascending colon, by the process of dehydration. Purgatives hasten insufficiently dehydrated, and, therefore, toxic material, out of the cecum, which has the power of selective absorption, into parts of the colon where toxins may be

absorbed, beyond the power of the liver to remove from the circulation, resulting in a general toxic state, indicated by the coated tongue, foul breath, headache and disordered digestion

Colonic stasis is very rare excepting in the cecum, where it is not uncommon. About 4 per cent of men and 14 per cent of women have cecal stasis, according to Fiddian (*loc cit*), who calls attention to the fact that Barclay, from long experience in radiology, declared that in the absence of mechanical obstruction, there are only 2 sites where stasis occurs, *ie*, the cecum and the rectum

Cecal stasis is indicated if, 24 hours after a barium meal, most of the barium remains in the cecum. The cecum is normally empty in the morning, and remains so until chyme begins to enter it 3 or 4 hours after breakfast. A patient, therefore, should be examined in the morning to detect a distended cecum, which at that time of day indicates cecal stasis. Patients suffering with this condition do not complain of constipation unless they also have dyschezia. They will believe that their bowels move normally, though the morning examination reveals a boggy and distended cecum.

Cecal stasis does not seem to be sufficient in itself to cause other abdominal pathology, but the fact that, accompanied by a ptosed right colon, it is an ever present associate of other abdominal conditions which bring the patient to the gastroenterologist and abdominal surgeon, indicates that a causal relation must exist

In quadrupeds the colon is suspended in its entire length by a mesocolon from the dorsal parietes, and is supported ventrally by the anterior abdominal wall, which prevents undue tension on the mesocolon

Man, when he became a biped and took an erect posture, incurred a liability to certain diseases, some of which are femoral and inguinal hernia, hemorrhoids and varicose veins, all of which are unknown to quadrupeds

The intestines are also affected by the pull of gravity in a direction at right angles to that which existed when they were in the prone position, so that certain modifications in peritoneal arrangements have occurred in the course of evolution of the human race, to overcome the difficulties encountered

These changes can be followed in the study of the colon in the human embryo, which is first entirely free, but later changes to the partially fixed condition. The ascending colon is securely fixed to the parietes in only 75 per cent of cases, however. Mobility of the right colon, therefore, is a congenital condition, which Treves found in 26 per cent of bodies examined, and Pirie in 20 per cent of the bodies of children

It is in cases of mobility of the right colon that the overwhelming majority of pathological conditions of the abdomen develop, and so, when symptoms of chronic stasis of that part, plus pain, exist, Fiddian advises that a timely **colopexy** be performed, before they come to the operating table for much more serious operations

**CONVULSIONS.**—Convulsions, *per se*, are symptoms and as such are treated under the various conditions with which they are associated. Here has been reviewed the literature pertaining to toxic convulsions, tetany, and certain unusual manifestations of convulsions as they occur in infancy and childhood

**ETIOLOGY.**—Temple Fay (*Am. J. Psychiat.* 10:551 (Jan) 1931)

would accord the same importance to the convulsions associated with the onset of acute infections as to the chronic forms found in idiopathic epilepsy. There is a predisposing factor which is common to all convulsive attacks. Fay describes this as an imbalance of the body fluids, with resulting imbalance in the hydraulic pressure of the cerebrospinal fluids. He considers a convulsion as a normal mass reaction of the cortical motor areas and integrated levels temporarily deprived of inhibitory control and released to reflex activity by some intercurrent mechanism. Control of the 3 neural factors which are involved is essential in checking a convulsive attack: (1) diminishing or preventing the sensory impulse responsible for the motor reaction, (2) raising the inhibitory threshold, (3) depressing or destroying the motor elements responsible for the discharge.

Fay suggests that treatment be directed towards regulation of the water mechanism and this should be instigated early.

Of interest in this connection is the recent work of H. M. Keith (*Am J Dis Child* 41:532 (Mar) 1931) on experimental convulsions in animals. Convulsions were induced by means of thujone. Rapid dehydration reduced, to some extent, the susceptibility of the rabbit to such an experimental convulsion. Total deprivation of fluid for as long as 168 hours did not have a similar effect. Acetone, ethyl aceto-acetate and diacetone alcohol reduced the susceptibility of the rabbit to experimental convulsions. None of these drugs caused dehydration of the brain tissue.

R. Waitz (*Bull. Soc. de pédiat. de Paris* 27:382 (July) 1929) reports the case of a newly-born infant with cerebral birth injury and convulsions who

exhibited the pilomotor phenomenon. The infant was cyanotic and the breathing irregular for the first half-hour of life. The next 18 hours he appeared to be normal. After this he had convulsive seizures and cyanosis. During the convulsions, and at times independent of them, the pilomotor phenomenon was manifested. The hair of the scalp became stiff and straightened and the skin of the face and extremities had the appearance of chicken skin. During the interval between seizures the hair and skin appeared to be normal. The spinal fluid was bloody and the pressure high, but higher during convulsions, and still further increased during the pilomotor phenomena. Postmortem examination revealed peribulbar congestion, subtentorial hemorrhage and congestion of the choroid plexuses. The pilomotor musculature did not appear to be abnormal. This phenomenon could not be induced in normal infants by the application of cold, ether, or xylene to the skin or by the injection of epinephrin.

**TREATMENT.**—The use of phenobarbital sodium subcutaneously is recommended by P. Leitner (*Monatschr f Kinderh* 48:323 (Oct) 1930) in the treatment of convulsions in infants. He thinks it more efficacious than the rectal administrations of chloral hydrate. If successful results are to be obtained only freshly prepared solutions should be used. The dosages recommended are: infants up to 3 months 0.01 Gm ( $\frac{1}{6}$  grain), up to 6 months from 0.01 to 0.02 Gm ( $\frac{1}{6}$  to  $\frac{1}{3}$  grain); up to 12 months from 0.015 to 0.03 Gm ( $\frac{1}{4}$  to  $\frac{1}{2}$  grain), and in children from 2 to 6 years from 0.03 to 0.05 Gm ( $\frac{1}{2}$  to  $\frac{5}{6}$  grain).

L. R. Gowan (*Minnesota Med.* 13:874 (Dec.) 1930) reports equally good results in the treatment of convulsions

with the intravenous administration of sodium amytal.

#### **TETANY.—TREATMENT.—**

Three cases of "tetany" with markedly positive Chvostek's signs, carpopedal spasm and convulsions occurring in the first few days of life are described by M H Bass and S Karelitz (J A M A 97 1372 (Nov 7) 1931). All 3 vomited frequently from the first day on, their abdomens were markedly distended, and their temperature high. Recovery was prompt after intravenous and intramuscular injections of calcium gluconate. Blood calcium was determined in only 1 case and was 8.5 mg per 100 cc. The authors suggest that their cases may be of the so-called gastric tetany type due to the marked vomiting and the resultant loss of HCl.

Several instances are reported in the literature of an association of tetanic symptoms and edema in the newborn, both of which are relieved by calcium therapy. Such a case is described by W. R. Shannon (Minnesota Med 13 476 (July) 1930).

Tetany may occur without a lowering of the serum calcium, as for example in those cases due to persistent vomiting, hyperventilation or heavy ingestion of sodium bicarbonate. E. F. Traut and R. P. MacFate (J A M A 96 266 (Jan 24) 1931) have studied a case in which at all times the blood calcium was within normal limits and the guanidine bases of the blood were always increased. The attacks were controlled by calcium or by parathyroid extract—Collip. In view of the fact that hyperguanidemia has been found in parathyroidectomized animals, the authors suggest that its presence may have some etiologic significance in tetany. A. S. Minot and J. T. Cutler (Proc. Soc. Exper. Biol. and Med 26 607 (Apr)

1929) quoted by Traut and MacFate (*loc cit*) found the blood guanidine elevated in cases of eclampsia and pre-eclamptic toxemia. All of their patients had low blood sugar readings. The improvement of their patients by the intravenous administration of calcium gluconate appeared to be due to increasing the sugar of the blood.

The need for measurement in the dosage of ultraviolet radiation in the treatment of tetany is shown by the study of H. Bakwin and R. M. Bakwin (J A M A. 95 396 (Aug 9) 1930). There is an optimal range of dosage above which and below which the rate of rise in the serum calcium is slowed. A daily dosage of 2 minutes front and 2 minutes back at 50 cm is optimal unless the burner is badly deteriorated.

A. Wittgenstein and A. Gaedertz (München med Wchschr 77 2183 (Dec 19) 1930) have used successfully intramuscular injections of calcium gluconate in the prevention and treatment of tetany in parathyroidectomized dogs.

N. W. Clein (Am J Dis Child 41 213 (Jan) 1931) emphasizes the need for individual adjustment of viosterol according to the infant's "type, rapidity of growth and development." He cites 2 instances in both of which, the patient, receiving viosterol, 10 and 15 drops daily, respectively, developed tetany. In each, tetany was relieved by increasing the dose to 30 drops daily.

#### **CORNEA.—HERPES ZOSTER OPHTHALMICUS.—Treatment.—**

The course of ophthalmic herpes is illustrated by 6 cases reported by R. I. Lloyd (Am. J. Ophth 14:601 (July) 1931). Herpes zoster ophthalmicus is characterized outstandingly by lowered corneal sensitivity. The eye symptoms

are secondary to the action of the virus upon the Gasserian ganglion, and are due to trophic changes with secondary infections, while the milder febrile type is the result of direct action of a specific virus upon the end-organs and other tissues of the cornea, with secondary infections. Lloyd considers the **constant covering of the affected eye** the most important step in the treatment for herpetic cases and the application of **radiant dry heat to the open eye** as next in importance.

**KERATOCELE.—Treatment.**—H. M. Emmons (Am J Ophth 14 1014 (Oct) 1931) reports a case of keratocele 6 mm in diameter caused by a piece of hot charcoal and associated with acute secondary glaucoma. Treatment by the use of a **fascia lata graft** resulted in immediate relief of pain and prompt cicatrization. Tension became normal and 1 year later the vision was  $\frac{20}{70}$ . He concludes that (1) fascia lata graft can be used to repair an extensive keratocele; (2) mechanical means can relieve a vasomotor type of glaucoma caused by the inhibition of the vasoconstricting mechanism, or by a paresis of the sympathetic nerve causing a stasis of the intraocular blood-vessels, (3) autogenous fascia lata is well tolerated in the eye for at least 2 weeks, (4) fascia lata should be considered for repair work on cornea and sclera which is too extensive for conjunctival flaps.

**TRANSPLANTATION OF CORNEA.**—A case of transplantation of the human cornea which was partially successful is reported by B. W. Key (Arch Ophth 5:789 (May) 1931), who transplanted the cornea of a man 32 years old who had a small choroidal sarcoma, to a man 26 years old who had an opaque cornea caused by a steam explosion 2 years earlier.

In each case the conjunctiva was dissected 4 mm from the limbus and the cornea incised at the limbus with a keratome, cataract knife and scissors. The graft was retained with scleral sutures. Nineteen months later perception of hand movements existed.

**TRAUMA.—Bee Sting.**—C. A. Young (Am J Ophth 14 208 (Mar) 1931) reports a case in which the cornea was penetrated by 2 bee stings. He succeeded in removing the stings under local anesthesia. He states that bee stings of the eye cause a marked local reaction which is evidenced by conjunctivitis, keratitis, hypopyon, iritis, cataract, perforation of the globe, glaucoma, and change in refraction. The general reaction is also severe with diarrhea, disturbance of heart action, fever, delirium and at times death. Bee stings contain poison and are probably never absorbed by the tissue.

**TUBERCULOSIS.**—W. Courtin (Arch f Kinderh 93 188 (May 15) 1931) reports a case of tuberculosis of the cornea in a nursing, aged 8 months. At the age of 4 months a primary tuberculosis of the skin, demonstrated by microscopic examination and by skin tests, had been observed. The mother had an open tuberculosis. Tuberculosis was spread to the cornea by way of a hand-borne infection. Hematogenic dissemination produced a tuberculous meningitis that ended fatally.

**TUMORS.**—A case of *epibulbar nevocarcinoma* with almost total corneal involvement is reported by Ramon Castroviejo, Sr and Jr (Am J. Ophth 14 757 (Aug) 1931). Pathological report of the sections suggests that possibly, contrary to the generally accepted idea, most of the tumors described in the literature as *epibulbar melanosarcomas* are really *nevocarcinomas*.

**CYANIDE POISONING.—**

**ETIOLOGY.**—A number of cases of acute nonfatal food poisoning occurring with any definite, traceable cause are described by H. Williams (J. A. M. A. 94:627 (Mar. 1) 1930). He believes that in many instances this poisoning was due to the use of silverware which had been cleansed with a polish containing sodium cyanide and states that it is a common practice, especially in hotels and eating places, to use a silver polish containing a large amount of this material as it quickly removes all tarnish. In checking his theories with various hotel managements, he found that there had been numerous com-

plaints of obscure food poisoning which in every case had been traced back to the use of silverware that had been treated in this manner. Now the City of Newark and the State of New York have banned, in all eating houses, the use of any polish on silverware which contains sodium cyanide.

**TREATMENT.**—M. Schmidt (Ugeskr. f. Læger 92:548 (June 5) 1930) obtained such excellent results after an injection of sodium thiosulphate that he believes this to be the only permissible method of treating cyanide intoxication. He states that Feyerabend's results with this treatment are even better than his own.

**D**

**DEAF-MUTISM.**—The importance of the education of the deaf is emphasized by the report of the Berlin correspondent of the American Medical Association (J. A. M. A. 92:1203 (Apr. 6) 1929), who details the provisions for the care of deaf-mutes and persons hard of hearing in Germany as developed in recent years. In 1912, there were in Germany 123 deaf-mutes per 10,000 inhabitants in the rural communes, 59 in the small cities, and 37 in the large cities. The condition is congenital in about 10 per cent. of cases, especially in regions in which goiter and cretinism are prevalent. The distribution of deaf-mutism varies with the locality.

The crusade against infectious diseases and the progress of medicine have brought about a distinct retrogression. In 1871, there were in Germany 97 deaf-mutes per 10,000 population; in 1900, there were only 86, and in 1925, only 6.4. Those who are

merely deaf have been included in the last mentioned figures.

The basis for the care of deaf-mutes is the census of such persons; more particularly, during the earliest years. The list of deaf and dumb children of school age has been kept up to date in Germany since 1902. The health officers throughout the country inquire into every case that becomes known and make a report on a prescribed form. The education and training of the deaf and dumb children who are found worthy take place in the institutions for deaf-mutes. There they acquire the necessary schooling and are prepared for some occupation. In 1923, there were 78 such institutions in Germany. The institutions belong to the various German states or communes, or they are administered by societies or by church or lay organizations of various kinds. Their education, which is in the hands of a specially trained teaching personnel, comprises, above all, instruction in



language, the endeavor being made to substitute, as far as possible, oral language for the sign language formerly employed. The industrial training is extensive. It is given by special teachers and artisans, who receive state awards for particularly good results from their instruction.

The federal law pertaining to the care of deaf-mutes may be outlined as follows. There are certain fundamental provisions contained in the *Bürgerliches Gesetzbuch*, or civil codex, and in the *Reichsversicherungsordnung*, or federal insurance law, though the latter concerns only those carrying compulsory insurance and who, by reason of disease or industrial accident, have become deaf and dumb or hard of hearing. Since 1924, the care of needy persons is based on the federal decree concerning such matters, together with the expositions thereto issued by the federal ministries of the interior and of labor. These regulations contain also provisions for deaf-mutes and persons hard of hearing. The care is an obligation of the *Fürsorgeverbände* (leagues), which are legally organized public bodies. The federal law pertaining to juvenile welfare, enacted in 1922, made provision for the care of minors. Provisions for deaf and dumb children had been made much earlier by the various German states. In Prussia, there was enacted, in 1900, the *Fürsorgeerziehungsgesetz*, and, in 1911, the law pertaining to the education of deaf and dumb children. According to the last mentioned law, the communal league (*Kommunalverband*) is under obligation to place in institutions for deaf-mutes all deaf and dumb children of school age.

State care of deaf-mutes is aided, to a great extent, by private charity or voluntary organizations. In addition to

the private institutions for deaf-mutes, there are about 40 German societies that care for and aid in the industrial advancement of adult deaf-mutes, for example, by securing them some form of occupation. The deaf-mutes have a league of their own, the *Reichsverband der Taubstummen*, which publishes a journal for deaf-mutes and aids needy members. The league of German teachers of deaf-mutes (the *Bund deutscher Taubstummenlehrer*) holds its regular meetings, and, with the aid of their special journal, *Blätter für Taubstummenbildung*, advances the cause of instruction of deaf-mutes.

The care of persons who are hard of hearing is of more recent origin. No statistics have been taken as yet. No legal provisions for the education of children who are hard of hearing have been made either by the federal government or by the individual states. In general, the obligations in regard to school attendance are the same for children who are hard of hearing as for normal children, however, in Prussia, on the basis of the law of 1927 in regard to school attendance, certain exceptions are made. The society of teachers of the hard of hearing (*Schwerhörigen-Lehrerverein*) has demanded repeatedly that special legislation be enacted with regard to the schooling of children who are hard of hearing. Saxony has 3 and Hamburg 1 state school for pupils who are hard of hearing. The remaining German states have 16 public institutions of this kind, with about 1400 pupils. In 1927, there were in Germany 23 schools for pupils who are hard of hearing, and 6 *Sprachheilschulen*, or schools for children with defective speech, in which an endeavor is made to remedy, through medical aid, existing speech defects. Furthermore,

Berlin, Dresden and Hamburg have opened continuation schools for pupils who are hard of hearing. In these schools, the remnant of hearing is developed as far as possible, and, in supplementary aid of remaining audition, instruction is given in lip reading in accordance with the *Horsehmethod*, a method that utilizes both audition and vision. These schools also provide instruction in manual training. In Berlin-Charlottenburg and in Hamburg, official bureaus of vocational guidance have been opened for persons hard of hearing. The correct choice of a vocation is of great importance for persons thus handicapped.

### DEAFNESS. —SOCIAL ASPECTS OF THE DEAFENED.—

Because of the tremendous *economic importance* of such an infirmity, much attention has been given to the training of the hard of hearing. Such organized efforts as have been referred to under deaf-mutism, both in America and Europe, illustrate the value of such work. However, in considering the economics of the afflicted deaf, Wendell C. Phillips (Auditory Outlook (Oct.) 1931) emphasizes the value of lip reading. More than 40 years of practice in the field of otology have taught Phillips that lip reading is a boon to 3 classes of persons.

1 The *deaf*, who are by its means brought closer into the common experiences of human intercourse. **Lip reading** for the deaf is usually accompanied by **instruction in speech**. This special education has been developed through more than 500 years of experiment and practice—it has reached a high degree of efficiency and should be made available to the little deaf child as soon as his sensory deficiency is discovered.

2 The *adult*, born with normal hearing, educated as a normal hearing person, using normal speech, but having suffered some impairment of hearing, should study **lip reading**. He will, as a rule, make better progress if he gets hold of his lip reading while he still has a considerable amount of hearing. The only exceptions should be persons who have defective vision.

3 The *child* with incipient but progressive hearing impairment. **Lip reading** will conserve his speech, bring school and college within his powers, and when he has received intelligent **vocational guidance**, will assist him to maintain himself in his chosen calling, as well as in his general social relationships.

The *economics of early lip reading* for all who experience impairment of hearing may be summarized accordingly, as promoting

1 A higher level of general health through diminishing nerve strain.

2 The mental discipline of eye training and alertness.

3 Improved mental hygiene through happier social intercourse and self-expression, leading to fuller emotional satisfactions.

4 A prime force in the readjustments so frequently indicated in hypacusia.

5 A bond of understanding between patient and physician.

6 Smaller expenditure for instruction to the adult.

7 Reduction of the cost of education for the school child with impaired hearing.

Furthermore, Phillips states that the fact should not, incidentally, be lost sight of that children consider lip reading a delightful game, that their hearing school-fellows admire them for their skill, and that adults find a genuine cul-

tural stimulus in their lip reading classes

In conclusion, the physician renders a definite public service when he advocates lip reading to his hard of hearing patients, to their friends, to other physicians and to school boards. He can and should lend a hand to the qualified hard of hearing teacher of lip reading—and by *qualified*, is inferred not only the teacher well-grounded in pedagogy and well-trained in her specialty, but also one who has made her own successful rehabilitation and who handles her own hearing problem intelligently and convincingly. The physician who advocates *early* lip reading will not only serve his community by lessening human wastage, but he will also receive the reward of an incalculable gratitude.

In an analysis of 325 cases of *chronic deafness* seen during the year of 1930, W. V. Mullin (Illinois M J 60.70 (July) 1931) found but 25 per cent who could be relieved by treatment and even among these improvement in some cases would be doubtful. He regretted his reputation as an aurist, because the other 75 per cent, in which advice as to lip reading and hearing aids was given or an institute for the congenitally deaf children recommended, the advice was not well received and, in the majority of instances, not followed.

The hard of hearing are deserving of especial consideration and need of treatment of some kind—especially psychological. The physician must compete with quacks and charlatans who empty the pockets of the deafened because they offer them hope and perhaps indulge in a bit of suggestive therapy.

Some of the most discouraging situations the otologist has to deal with are those that relate to the treatment of patients with chronic marked and progres-

sive deafness. In most instances the otologist is compelled to give a poor prognosis, not only as to prevention of further progress of the illness, but an even worse prognosis as relates to improvement of the condition as found at the time of examination. Reeducative processes seem to offer the best solution, few honest otologists are inclined to treat progressive deafness with the catheter, by pneumomassage, etc. In his booklet (Oxford University Press, 1931), Cathcard offers for the consideration of the profession an educative technic by means of a complicated instrument, the *electrophone* of Zund-Burguet, which reproduces the sound vibrations of the whole gamut of the human voice and thus gives the requisite *physiologic stimulus* to the ear. The author's standing in his own country is good. The improvement that his patients have obtained with this method is impressive. It would be comforting to hear from others who have had results as fortunate.

### DELINQUENCY (JUVENILE).

—The majority of reports of the last year indicate that the number of instances of juvenile delinquency is increasing. It is difficult to determine whether this is an actual increase or is the result of added interest and facilities for the detection and study of the criminal acts of children. The problem of treatment has been approached from many angles: (1) that of the law which has established additional juvenile courts and bodies of trained social workers to investigate each juvenile crime; (2) that of the physician who has been searching for a physical basis of delinquency; (3) that of the psychiatrist who has attempted to explain the child's behavior on the ground of mental de-

ficiency; and, finally, (4) that of the psychologist and social worker who have been investigating the environment and the social adjustment of the child in relation to his delinquency. It has been suggested that the ideal method of approach is the coordination of the efforts of all these workers in the so-called "child guidance clinic."

I S Wile (Am J Dis Child 40 1076 (Nov) 1930) quoted the statistics of certain investigators to the effect that only 11 to 15 per cent of juvenile delinquents are psychopathic. Mental deficiency of such a group is more prevalent than in normal children, but certainly it does not account for all the youthful criminal acts. The author stressed the importance of considering many actions of a delinquent nature as expressions of behavior problems of earlier life, and as the desire of the child to adjust himself to his surroundings. The biologic urges of self-protection, self-development and self-advancement which an individual may desire to fulfill may occasionally lead to behavior which the laws of a community have declared to be "offenses" or "delinquency." Any isolated act of a child may be only his expression of a larger purpose or scheme of adjustment.

Following the study of 1300 children who had been brought into court with various charges of delinquency, G Heuyer and Mme Roudinesco and M Néron (Rev internat de l'enf. 10:223 (Oct) 1930) were able to group most of the offenders as follows: (1) Those who had had improper care and training at home; (2) those with definite organic nervous disorders; (3) feeble-minded children; (4) true criminal or perverted types.

The relation of feeble-mindedness to delinquency was the basis of a study by

R G Gordon, R E Thomas and E G Greenall (Brit M J 1 490 (Mar 15) 1930). Burt's statistics had indicated that only 7 per cent of juvenile delinquents were mentally defective, but the authors believed this was too low a figure and they attacked the problem from the other angle, *ie*, the study of delinquency in a group of definitely retarded children. A group of 100 children were suspected by their teachers as being mentally retarded; 84 of these were found to have intelligence quotients between 60 and 90; 12 between 90 and 100, and 2 above 100. Of the entire group, 64 had shown good conduct in school, 36 had not. Twenty-four were distinctly asocial, and 25 had had the history of unsatisfactory conduct at home. In a large proportion of the children who had problems of misconduct, the home life was unsatisfactory; either there were disturbed parental relationships or the parents were psychopathic. In addition, there was the observation that 90 per cent of these patients succeeded in adapting themselves to their environment in later life. Conversely, the authors concluded that the majority of behavior difficulties apparently occurred early in the life of the mentally retarded individual.

In regard to other causal factors of delinquency, S. K. Smith (J A. M. A 94 710 (Mar. 8) 1930) observed a greater number of certain physical defects among a group of delinquent children than in a similar normal group. Such defects included underweight, anemia, carious teeth, chorea, pathologic chest conditions. The writer did not venture an opinion as to the importance which physical defect might assume in causing delinquency, but believed that it was one factor which should never be overlooked by any child guidance clinic.

Conversely, certain behavior difficulties may seriously affect the health of the patient. This has been illustrated by I. P. Bronstein (Arch Pediat 47: 615 (Oct) 1930) with the case histories of several children who had definite clinical syndromes simulating acute illnesses but who probably had, as the underlying disturbance, certain mental conflicts which had arisen from jealousy, from the desire of attention, and the like. For instance, 1 child had definite epileptiform convulsions which were somewhat atypical but seemed to have a definite organic etiology. Subsequent inquiry, however, indicated that the child resented a withdrawal of his parents' attention from him to his baby brother and he was attempting to regain the center of attraction. Social readjustment put an end to the patient's illness. Other instances were cited in which unsuitable environmental conditions led children to complain of symptoms which sometimes led to prolonged medical treatment and even surgical operation.

It cannot be doubted that some instances of juvenile delinquency can be traced directly to faulty training in the home. In accordance with this idea, H. Hanselmann (Rev internat de l'enf 9: 27 (Jan); 118 (Feb) 1930) concluded from a study of 1500 delinquent children that home training was the most important factor in control of delinquency among children. According to Hanselmann, further efforts must be directed towards **parental education** if the number of youthful misdemeanors is to be reduced.

Has the absence of one of the parents from the home any bearing on delinquency among children? A study to answer this was made by S. B. Crosby (J. Juvenile Research 13: 220 (July) 1929)

in a group of 314 delinquent boys. A broken home, in which the mother was usually left to care for the children occurred more frequently in this series than in a control group of normal children, but the statistics did not indicate that the presence of both parents always insured a more satisfactory environment and training of the children.

**DEMENTIA PRECOX.** See SCHIZOPHRENIA.

**DERMATITIS.—ETIOLOGY.—***Pollen dermatitis* has been shown to be a contact dermatitis and is not of allergic origin, according to A. Brown, E. L. Milford and A. F. Coca (J Allergy 2: 301 (July) 1931). The dermatitis is caused by the pollen oil and not by the atopen which is somewhat soluble in the oil.

Specific reactions elicited in ragweed-sensitive individuals by tests with ragweed pollen oil are due to the contamination of the oil with the atopen. Pollen dermatitis occurs after an incubation period of from 1 to 5 weeks, whereas the specific skin test with pollen extract by the intradermal method in sensitized individuals, is immediate. Ragweed-sensitive hay fever subjects do not give a specific reaction to the pollen oil after it has been dialyzed through a rubber membrane. Pollen oil freed from the atopen caused dermatitis in 15 per cent of hay fever subjects, in 15 per cent of atopic persons not subject to hay fever, and in 15 per cent of nonatopic persons.

Hypersensitiveness to pollen oil resulting in contact dermatitis (*dermatitis venenata*) is thus seen to exist without relation to atopic susceptibility of the individual and pollen dermatitis is to be grouped with the dermatoses caused by poison-ivy, sumac and primrose.

**DIABETES INSIPIDUS.**—F N. Allan and L G Rowntree (Endocrinology, 15 97 (Mar-Apr) 1931) present a very thorough review of the entire subject of diabetes insipidus, particularly in regard to its relation to diabetes mellitus. They point out that many cases reported, particularly those in the German literature, in which these 2 conditions have been thought to co-exist, have been studied with inadequate laboratory examinations and so the diagnosis of diabetes mellitus cannot be definitely established. Two cases of diabetes insipidus are cited in which diabetes mellitus has coexisted. These are the only cases in the 100 cases of diabetes insipidus seen at The Mayo Clinic and they feel that the total number of authentic cases associated with these 2 conditions is probably not greater than would result from pure coincidence. They consider, however, the theoretic possibilities of some common factor in the production of both conditions and feel that to attribute both of the diseases to pancreatic lesions is unjustifiable, in the light of modern knowledge, but that they both may be due to some intracranial lesion. However, from a practical standpoint, it is significant that the disturbance of carbohydrate metabolism can be controlled by diet and insulin and that the use of pituitary extract for polyuria does not interfere with the effectiveness of insulin.

**TREATMENT.**—T B. Fitcher (Ann Int Med. 5 566 (Nov) 1931) covers extensively the history of the development of the knowledge of diabetes insipidus and in regard to treatment of this condition suggests the following

1. If the patient has a positive Wassermann, **antiluetic treatment** should be instituted, as the polyuria might be

dependent upon a gumma of the mid-brain or upon a basilar syphilitic meningitis

2 **Surgical interference** is often indicated where there are neighborhood pressure symptoms, such as headaches, ocular palsies, bitemporal hemianopsia, and choked discs. An early operation may prevent total blindness, even though it may not materially influence the polyuria

3 The hypodermic use of 0.5 to 1 c.c. (8 to 16 minims) of surgical **pituitrin** often relieves the distressing *thirst* and *polyuria*. The dosage and interval between doses has to be worked out in each individual case. Usually the effect of an individual dose does not last longer than from 4 to 6 hours. Following basilar tumor operations, a distressing diabetes insipidus may develop when it did not previously exist. Polyuria and polydipsia will then disappear; if they do not, **pituitrin** is sometimes effective. In these cases a tampon of cotton soaked with pituitrin may be inserted into one nostril, or 1 c.c. (16 minims) of pituitrin may be diluted with 30 c.c. (1 ounce) of normal salt solution and frequently sprayed into the nostrils.

In some instances, it is found that pituitrin has little or no effect in the control of polyuria and the author cites Elmer's classification based on an etiologic and therapeutic viewpoint, which is as follows.

(a) Cases due to destruction of the posterior lobe of the hypophysis. Here the posterior lobe extract fails entirely or only in part to sensitize the regulating centers for water and salt in the hypothalamus. In these cases pituitrin has a definite, though transitory therapeutic effect, the explanation for this lies in the fact that the regulatory centers in the hypothalamus are intact.



(b) Cases due to destruction of the water and salt regulatory centers in the hypothalamus. In these the secretion of the posterior lobe is still produced, but it cannot sensitize the hypothalamic centers because they are destroyed. In this group the pituitrin has no effect whatever, since the regulatory centers in the hypothalamus are destroyed and are incapable of sensitization.

(c) Cases in which there is an interruption of the communicating nerve fibers connecting the hypothalamus (tuber cinereum) and the posterior lobe of hypophysis. This group, they state, is insufficiently understood and requires further investigation. The therapeutic effect of pituitrin is not stated.

If the views of these authors be correct, the failure of pituitrin to act therapeutically may be referred to those cases where the so-called center or centers are destroyed.

The efforts of many laboratory men have been directed during the past year to the study of diabetes insipidus from the chemical aspect and one of the most interesting of these is reported by Max Gradwohl (*Deutsche med Wchnschr* 56 1700 (Oct 3) 1930) in a woman in whom a true diagnosis of diabetes insipidus was made. The blood showed a marked increase in sodium. An increased capacity to bind water was demonstrated in the normal erythrocytes. Under the influence of a preparation of the posterior lobe of the pituitary the potassium value returned to normal and the sodium rose slightly while the red cells no longer showed swelling.

A significant observation was made upon two subjects, without metabolic disease in whom injections of posterior lobe of pituitary were given and were not followed by any change of note in the potassium and calcium values.

**DIABETES MELLITUS.—ETIOLOGY.**—While much has been written about the pathological findings in cases of diabetes mellitus, it must frankly be admitted that the exact cause or rather the *modus operandi* of the production of the disease remains unknown. It is obviously due to some defect in the insulogenic mechanism, but whether that be a defect in the islands of Langerhans or to some inhibitory or deficient stimulation from the central nervous system remains obscure in many cases. There are certain cases which at autopsy show definite change in the islet tissue, but there are many more and, indeed, some of the severest clinical cases, in which no characteristic pathological change can be demonstrated.

This has led to the theory that there are 2 types of diabetes: (1) "Insular diabetes" with definite changes in the islands demonstrable at autopsy. This type responds readily to insulin. (2) The so-called "central diabetes," which is thought to be due to some lesion in the central nervous system which either inhibits the secretion of insulin or stimulates the secretion of its antagonist epinephrin. These cases are supposed to be more resistant to insulin therapy but unless care is taken, as stated elsewhere, all those cases in which there is any difficulty whatsoever in adjusting the insulin dosage will be classified as "central diabetes." Whether there are 2 such types of diabetes or not is still an open question.

The development of diabetes following pancreatitis severe enough to destroy islet tissue should occur if the first of these hypotheses is true. There have been comparatively few cases of pancreatitis followed with sufficient care to determine this fact. The 2 following articles in this neglected subject seem

to be of particular value in tracing the association of diabetes and inflammatory disease of the pancreas

J. S. Sweeney (*Endocrinology* 15:508 (Nov.) 1931) reports the case of a man 48 years of age, whose chief complaints were easy fatigue, frequency of urination, loss of weight, and slight discomfort at the end of the day. His mother and father both died of diabetes, as did an only brother. As a result of this family history, the patient had his urine examined 4 times a year and it was always found negative. When he presented himself for examination to the writer his urine showed 2 per cent sugar and the blood sugar was 187 mgms. per 100 c.c. The symptoms became progressive and were associated with icterus. A diagnosis of subacute pancreatitis was made. This was confirmed at operation and the surgeon found a diffusely hardened pancreas and performed a **cholecystojejunostomy**. The patient made an uneventful recovery and was able to continue sugar-free and with a normal blood sugar on a qualitatively restricted diet, whereas before operation he required a quantitative restriction of his diet and insulin. While this patient has been followed only a few months, it would seem likely that he had a diabetic tendency because of this family history and that the inflammatory condition of his pancreas impaired enough islet tissue to produce a true diabetes which was relieved when the pancreatitis subsided, but which left him still a potential diabetic.

F. B. Bernhard (*Klin. Wchnschr.* 10:632 (Apr. 4) 1931) reports that of 50 patients who in the last 20 years received treatment for acute pancreatitis and who recovered from the operative intervention, 3 have died of diabetes and in 2 the disease is present. This is

a morbidity of 10 per cent. Diabetes developed particularly in those cases in whom acute necrosis of the pancreas was followed by the expulsion of pancreatic sequestrum or in whom pancreatic fistulas persisted for a long period. But even after pancreatic necrosis of minor severity, the later development of diabetes may be expected. Sugar tolerance tests were made in 25 of the patients and 5 of these, or 20 per cent, showed curves typical of potential diabetes. These were observed mainly following acute pancreatic diseases in patients in whom during the operation the pancreatic disturbance presented a serious aspect or in whom after surgery a pancreatic fistula developed. The removal of a diseased gall-bladder at the time of operation did little to prevent the development of a lowered carbohydrate tolerance. In one case with relapsing pancreatitis there was observed that with the gradual destruction of the pancreatic tissue, there was a gradual progressive inability to utilize carbohydrates. Bernhard stresses quite properly the importance of subjecting these patients to frequent carbohydrate tolerance tests.

In the support of the "central theory" of diabetes, G. H. Tuttle (*New England J. Med.* 204:963 (May 7) 1931) accepts as true the hypothesis of MacLeod that insulin is produced through vagal stimulation of the islet tissue (probably that of the right vagus), and also the hypothesis that such action occurs as a result of the stimulation of a sugar center in the vagus nucleus of the brain by a rising blood sugar. He feels, however, that these 2 hypotheses do not help in an understanding of the diabetic state of glycosuria, ketosis and coma, for if slowly developing primary diabetes has at its beginning a slowly rising

blood sugar, which would theoretically stimulate the sugar center, the disease would be cured automatically. But if a break in this chain is imagined, such as a paralysis of the vagal filaments, then the ordinary picture of diabetes will develop, under such conditions nothing else could develop and this is the theory offered by the author to explain the development of diabetes.

Excessive stimulation, he states, never causes degeneration of organs but rather hypertrophy, so that the long continued stimulation from the sugar center cannot cause degeneration. Paralysis frequently produces atrophy and degeneration of the end-organs, but it has been pointed out that islet degeneration is not always seen even in severe diabetes and Tuttle (*loc cit*) feels that this is due to the humoral stimulation that these cells are subjected to.

Tuttle visualizes the paralysis of the nerve as brought about by a long continued overstimulation and feels that such a condition of overstimulation occurs from overfeeding in the ordinary case of diabetes. The long-continued high blood sugar lasting for months or years perpetually overstimulates the sugar center which, in time, overstimulates the vagal filaments, until partial or complete paralysis results from the progressing fatigue. He then visualizes a perfectly normal pancreas which cannot be stimulated because of vagal nerve paralysis. The mild cases are due to fatigue which, after rest caused by adequate diet and insulin, is overcome and these patients regain the ability to utilize more carbohydrates.

In the moderately severe cases the paralyzed nerve tends to recover some of its power through rest and these cases often improve. In the case of

"complete" diabetes, these fibers are destroyed and no recovery can take place. The author feels that there is another means of stimulating this flow of insulin, *viz*, by secretin, and he feels that the utilization of this action will be one of the future advances in diabetic treatment.

While there are many points in such a hypothesis which remain to be proven before it can be seriously considered, it is a pleasant realm of speculation and would seem to give some lead for etiological studies in the future.

P. B. Matz (Military Surgeon 68.591 (May) 1931) reports the result of his studies of 300 cases of diabetes in *ex-service men*. This is an extremely interesting study because of the fact that these cases all occurred within somewhat the same age groups and because of the fact that they were all more or less exposed to the same or comparative conditions before the development of the disease. Modern warfare has been cited as a possible etiological factor in the production of the increasing number of cases of diabetes because of the nervous strain to which these men were subjected, particularly those who were in the front line trenches, and secondly, the element of trauma and injury which has been shown by Joslin and others to be a possible factor in the precipitation of this disease. The evidence gathered by this writer has not borne out this supposition and he feels that these cases can be readily explained on the basis of constitutional predisposition, obesity or faulty metabolism. Twenty-eight per cent of this group gave evidence of diabetes after the age of 40; 71 per cent before the age of 40; while 2 members of the group of 300 were over 65 when the disease was first detected.

In considering the large number of cases developing before 40 years of age, it must be considered that this group is a group of ex-service men whose average age at the time this study was made was 33.7 years.

Another interesting finding is that only 5 cases, or 1.6 per cent, had clinical symptoms suggesting diabetes mellitus and that in this group of 300 there were 5 cases of renal glycosuria. An attempt was made to classify these patients according to their activity, and it was found that in 24 per cent of the group there was no limitation of activity, 30 per cent of the group slightly limited; 30 per cent greatly limited and 3 per cent were unable to carry on any activity. Unfortunately, it is not indicated in this article whether these patients were incapacitated because of diabetic conditions *per se*, or because of complications. Another interesting point that was developed was that those cases that showed a normal blood cholesterol content were more amenable to therapeutics and were easier to control than those cases where the blood content was above normal.

It has at times been supposed that diabetes in the negro was a very rare disease and that its treatment was quite different from the treatment of the same condition in the Caucasian. This, however, has not been the experience of men who have had large clinic experience.

E. J. Leopold (Ann Int Med 5.285 (Sept.) 1931) reports his observations in 100 cases of diabetes occurring in the negro seen at the Johns Hopkins Hospital. He has concluded that the disease is by no means a rare occurrence. He feels that syphilis is not an etiological factor in the cause of the disease or its progress and that the treatment of

the lues influences but little the diabetic condition. Only 4 per cent of his cases showed gangrene of the leg and 2 of these were complicated by lues. He concludes that "diabetes in negroes is not different in any way from the disease as found in white people." It does, however, present a social problem because of the economic and intellectual status of the average negro dispensary patient. However, it has been experienced in most diabetic clinics that a well controlled and trained negro diabetic is as easy to handle as is a diabetic of equal social status in any other race.

L. E. C. Wendt and F. B. Peck (Am J M Sc 181.52 (Jan.) 1931) analyze a series of 1073 cases of diabetes. There were twice as many females as males. The age of obesity was the age of diabetes, of arteriosclerosis and gangrene. Diabetes may follow excessive nervous and mental strain but this type is usually mild. Familial factors were found in 14.8 per cent and there is a much higher incidence among the more intelligent classes. Their series showed a higher percentage of syphilis than those of other observers.

**PATHOLOGY.—Arteritis.**—M. Labbé (Presse méd 39.257 (Feb. 21) 1931) in writing on diabetic arteritis states that it differs from syphilitic arteritis in its localization and the coats of the artery involved. Syphilis attacks especially the aorta, the larger arteries causing a panarteritis, while diabetes attacks the smaller arteries and causes an endarteritis.

There is no disease, he states, in which arteritis occurs as frequently as it does in diabetes. It occurs early and its frequency is not proportioned to the severity of the disease. It is less common in diabetes with nitrogen denutrition than in benign diabetes with denutrition.

Diabetic arteritis affects principally the lower limbs. He feels that a diet deficient in carbohydrates and high in fat may be a contributory factor by the development of hypercholesterinemia.

The first *symptoms* of diabetic arteritis are slight sensory disturbance, such as numbness of the extremities, sensations of cold, formication and cramps. These often occur at night. Later there are attacks of ischemia with severe pain and sensation of constriction, intermittent claudication is experienced during the day, arterial pulsations cease first in the dorsalis pedis, the posterior tibial and popliteal arteries. Oscillometry, whatever its deficiencies, is the best means of appreciating disturbances of arterial circulation in a limb.

The author speaks of the importance of x-ray examination for calcification of the arteries, but states that palpation or oscillometry are of more value in the prognosis.

He feels that it is important to supplement the arterial examination with an examination of the peripheral nerves, and points out that a conservation of the tendon reflexes means integrity of the central nervous system and the sensory disturbances must then be attributed to the circulatory lesions.

The author's conception of the pathogenesis of diabetic arteritis is as follows. The blood, which is abnormally charged with glucose, chronically irritates the intima and causes it to become thickened and slightly inflamed. Later, the cholesterol, which is in excess in the blood of diabetics, penetrates the intima and is there deposited. The deposits may be acted upon by therapy which reduces the cholesterolemia. Infiltrated into the intima and swelling it, the cholesterol is a primary factor in the production of circulatory disturbances.

It constricts the lumen of the vessel and is responsible for the ischemia and gangrene. Spasm and thrombosis play scarcely any part in the mechanism of arterial stenosis in diabetics. As there seems to be no relation between the calcium contents of the arteries and the blood calcium, a low calcium diet is unnecessary.

**Gangrene.**—H. F. Root (Arch Surg. 22:179 (Feb) 1931) feels that the immediate cause of the diabetic *gangrene* is avoidable. He reports 7 cases who had amputations of legs or toes, 3 had cut corns without precautions, clean hands and clean feet would have saved their legs. The fourth patient stepped on a nail and continued to work in spite of suppuration. The first had blisters due to tight shoes and the seventh walked barefooted in zero weather, striking his toe, without remembering any injury. So deficient was the sensation and so slight was the injury that resulted in gangrene.

Defective vision resulting in too deep cutting of corns, improper shoes causing trauma from pressure, unprotected feet and neglect of minor infections are causes that may be combatted by the education of the patients and by careful and energetic treatment by physicians. The feet of diabetics are vulnerable because they are mechanically deformed, particularly is this true after 50 years of age. Hammer-toe, made stiff by arthritic changes, causes abnormal points of pressure with the formation of callosities, these can be kept free from infection only if given proper care.

Bunions, with displacement of the great toes, not only produce abnormal points of pressure over the metacarpal-phalangeal joint but often cause soft corn on the inner aspect of the fourth toe and calluses on the dorsal and

under surface of the first toe, so that every bunion has at least 3 potential points of infection. Flat anterior arches result in calluses over the head of the metatarsals and the abnormal pressure causes perforating ulcers. When soft corns are infected, involvement of the joint is almost certain if healing has not occurred within 2 weeks.

Chronic infections of the feet are most important, 70 per cent of diabetic patients have *epidermophytosis*, while these lesions are not dangerous in themselves, they provide a portal of entry for infection.

Gangrene is precipitated by faulty care of vulnerable feet by patients enfeebled on account of age and handicapped by poor vision and defective sensation of the feet. To prevent the development of gangrene, the author recommends. Shoes that are long enough and soft enough, proper hose that are not too tight or too large, for wrinkling will cause blisters—medium weight cotton and wool stockings are ideal, and they should be changed daily, and of prime importance is the education of the patient.

**Wassermann Reactions.**—H. F. Root and G. A. Stuart (New England J Med 204 1179 (June 4) 1931) reported a series of 1078 blood specimens on which were carried out simultaneously a Wassermann, Hinton and Kahn test for syphilis, and also the blood sugar and cholesterol determination. They found that a disagreement in the 3 tests occurred in 59 cases. The largest number of doubtful tests were obtained by the Kahn and the least by the Hinton reaction. They found that neither the height of the blood sugar, the amount of blood cholesterol, or the presence or absence of acidosis or albuminuria had any tendency to definitely

produce false reactions in any of these 3 tests.

**COMPLICATIONS**—F. D. Murphy and G. F. Moxon (Am J M Sc 182 301 (Sept) 1931) report a series of 827 cases of diabetes, in 681 of which some complication was observed. They list 75 types of complications under 7 main heads, *vis* (a) Diabetic coma, (b) cardiorenal disease, (c) infections, (d) tuberculosis, (e) carcinoma, (f) syphilis, (g) miscellaneous.

There were no cases of rheumatic fever in the entire series, which again emphasizes the rarity of the condition in the diabetic and helps to explain the infrequent finding of a true endocarditis in these cases.

The author reported 40 cases of *pulmonary tuberculosis*, an incidence of 4.83 per cent, of these 16 died. Of the 40 cases, 14 were considered free from tuberculosis when the diabetic condition was discovered, while 26 had both diabetes and tuberculosis when the diagnosis of the former disease was made. Although the incidence of pulmonary tuberculosis is not much greater among the diabetic than the nondiabetic, the death rate is considerably greater in the diabetic group.

*Malignant disease* occurred 8 times in the group, 1 being a case of carcinoma of the head and tail of the pancreas. The mortality from malignancy was 50 per cent.

They had 33 cases of diabetic *coma*, of which 20 were uncomplicated and of this group 18 recovered. The secondary group with complications showed a mortality of 10 deaths in 13 cases. The mortality rate from 1926 to 1930 was much better than for the preceding 4 years, due to a better understanding of insulin therapy and larger use of fluids in the treatment of coma.



They had 72 cases of *gangrene* with a mortality of 48.6 per cent. Of this series, 40 had *heart disease* and 22 of these died of cardiac failure. There were 16 cases of *pneumonia* with a death rate of 87.5 per cent, as compared with a mortality of 54.5 per cent in cases of pneumonia in nondiabetics, 37.4 per cent of this series were *syphilitic*. Antisyphilitic treatment was followed by apparent recovery in 2 cases, although the etiological importance of syphilis as a factor in causing diabetes has yet to be proven.

Miscellaneous complications totaled 210 and are rather unimportant in themselves, except that they represent a serious problem in the management of the disease and, unless recognized and controlled or corrected, lead to more serious conditions. Murphy and Moxon (*loc cit*) discuss the importance of a thorough routine examination to discover any hidden complications. This, of course, should be an annual procedure in the correct management of any case of diabetes mellitus.

Finally, the mortality was 35.7 per cent for the group, which is composed of routine admissions to a ward service, as contrasted with that of a group of private patients which had a mortality of 21.5 per cent. The difference they feel is due to the difference in co-operation, intelligence and economic conditions.

**Coma.**—As has been stated before, coma as a complication and cause of death in diabetics is rapidly becoming less. This is due to 3 factors:

1. Education of the physician to appreciate that satisfactory diabetic management means keeping the patients on a diet which is satisfying to them and which will not tend to produce acidosis because of its high fat percentage, and

also the use of adequate insulin when indicated.

2. Simplified laboratory tests for blood sugar and plasma CO<sub>2</sub> determinations and greater accessibility of laboratory facilities.

3. Education of the patient, and this is probably the greatest single cause of the reduction of the number of cases of coma. Patients and their families are taught the early symptoms of coma and the emergency measures which should be taken to combat them. They are also taught the importance of good diabetic hygiene and frequent examinations, but, above all, they are taught to call the physician if any untoward symptom develops.

This results in cases of mild acidosis being seen early and the development of coma prevented by prompt treatment. Cases of diabetics admitted to the hospital in coma have been increasingly infrequent during the past years in the experience of the author, and in the last 100 cases admitted to the hospital, there were only 4 cases of diabetic coma among adults and 3 among children.

In spite of present knowledge of the treatment of coma, there are always a certain number of cases of diabetic coma who die. These are usually associated with anuria, due possibly to extreme irritation of the kidney in its attempt to eliminate the ketones in the body. It has been shown by several investigators during the past few years that severe ketosis can exist without ketonuria, and, indeed, some feel that the disappearance of the acid bodies from the urine with blood chemistry indicating severe acidosis, is a forerunner of a complete anuria.

G. Pellegrini (*Riforma med.* 47:869 (June 8) 1931), in discussing diabetic coma, states that it may be complicated

by a true renal insufficiency which would give rise to the clinical picture of uremic coma. He feels also that in other cases of diabetic coma signs of hepatic insufficiency may be noted and believes its characteristics are the lack of ketogenesis, with a more or less accentuated reduction of the alkali reserve. He gives the pathological findings of such a case which showed grave changes in the liver, and which before death presented rather complex comatose manifestations. The treatment of diabetic coma tends to become more and more standardized among those clinicians who treat large numbers of diabetics.

The changes in the blood urea occurring in diabetic coma have been studied by M. Labbé and R. Boulin (Ann de méd 9 386 (Apr) 1931). Their conclusions are that in a certain number of cases, approximately half, diabetic coma is accompanied by a moderate azotemia, the amount of urea being about 0.1 Gm per 100 c.c. This is associated with a decrease in the amount of urine excreted and with albuminuria and cylinduria. Its presence does not change the other classical characteristics of diabetic coma, notably the alkali reserve, the hyperglycemia and glycosuria. The amount of chlorides is markedly decreased in the urine and somewhat decreased in the blood. The amount of acetone bodies is small in the urine, however, in none of the series were they completely absent. The clinical signs are not noteworthy. It seems to these authors that azotemia is related to the degenerative lesions in the convoluted tubules, probably caused by the effort to eliminate the acid bodies. The change in the blood urea occurs early and is of great prognostic value. Cases of diabetic coma complicated by retention of urea terminate fatally twice as fre-

quently as those without azotemia. The continued high blood urea after 24 hours of treatment is a highly ominous sign. Death may occur from irreducible acidoketosis, from heart failure, or from observed conditions that have been designated as uremia, but which the authors feel are still of undetermined origin.

From the 2 articles quoted above it is apparent that diabetic coma is a complex comatose condition and that other laboratory studies than the plasma  $\text{CO}_2$  would be of great value in determining the prognosis and to some extent in guiding the treatment of their case.

**Dental Complications.**—It is pleasing to note the dental interest in various medical conditions and a very interesting analysis of 138 diabetic cases is presented by J. B. Williams (Am J M. Sc. 182:807 (Dec) 1931). In this group, 135 showed *pyorrhea* at the time of examination or gave a history of having had *pyorrhea*. The author distinguished 2 types of oral involvement in diabetes, the first seen in those having developed diabetes. These patients presented the following picture: The teeth were loose; the gums were hypertrophied, inflamed and dark red, ulcerated and sometimes covered in spots with grayish areas of necrotic tissue. While it resembles to some extent Vincent's infection and mercurial poisoning, it has such distinctive characteristics of its own that it is believed to be a clinical entity. On the other hand, patients under diabetic control present a somewhat different appearance. Their teeth are firm, the mucous membrane while soft, flabby and spongy, presents no areas of ulceration; and the gums, as a rule, do not recede; but there is extensive loss of alveolar bone, together with deep pockets, but with little or no pus

formation About one-half of the patients reported in this series were edentulous, but gave a history of *looseness of the teeth* which was noticed prior to, or at the time of the discovery of the diabetes This looseness became more marked and finally necessitated extraction He presents some theoretical reasons for this frequent pyorrhea and the apparent lack of local resistance in the diabetic mouth and feels that the elimination of dental foci of infection is of great importance in the routine treatment of diabetes

This is one of the few statistical reports presented on this somewhat neglected aspect of diabetic care. It would seem that the incidence of pyorrhea in this series was a good deal higher than seen in the average run of clinic patients

The author's views on the importance of removing these foci of infection cannot be over-emphasized and the dentist should recognize the necessity of co-operating with the physician in the management of this condition and, indeed, an alert dentist may be the first one to recognize the systemic origin of certain types of pyorrhea

**DIAGNOSIS.**—While the diagnosis of diabetes is usually made by finding glycosuria and hyperglycemia or as a result of a sugar tolerance test, it is well to bear in mind that another laboratory test is available which is of great aid in definitely diagnosing the suspected case of diabetes This is the determination of the *respiratory quotient* which, while it is a hospital procedure and probably never will become an office routine, yet, is of great value in doubtful cases and should be utilized whenever available in those occasional cases which present a problem in diagnosis.

Wishnofsky and Byron (Arch Int.

Med 48:351 (Sept) 1931) emphasize this point They show that the renal threshold for dextrose varies from 45 to 348 mgms per 100 c.c. and that glycosuria may occur without hyperglycemia or true diabetes They also speak of the cases with high threshold and a hyperglycemia without glycosuria. They point out that hyperglycemia or even a high curve following the ingestion of 100 grams of glucose may be present in such conditions as hypertension, nephritis and hyperthyroidism, and at times may be high enough to suggest a diabetic curve In these cases they feel that a respiratory quotient test is of great value. If after the ingestion of an adequate amount of carbohydrate the respiratory quotient curve rises to 0.88, it is indicative of a normal secretion of insulin Lower figures indicate hypoinsulinemia

The incidence of achlorhydria in diabetes has been investigated by I. M. Rabinowitch, A. F. Fowler and B. A. Watson (Arch Int. Med. 47:384 (Mar) 1931), who report the literature on this rather interesting finding.

Other investigators have felt that the presence of a true achlorhydria was also associated with a severe diabetes and that achlorhydria was apt to be found in diabetics who have the disease over a period of 3 or more years. In order to collaborate this work, 100 diabetics were studied at the Montreal General Hospital. These tests were made by single estimation, following an Ewald meal, which they feel yields the most satisfactory result in the majority of cases. These investigators were able to show no relationship between the duration of the disease and the acidity, nor did they feel that there was any relation between the severity of the disease and the level of free or total acidity. They could find

very little association between the age of the person and the acid readings, taking into account the fact that the total and free acid is apt to be rather low in persons beyond middle age. They state that the experience of many workers and their own analysis of normal persons with the Ewald test meal shows an incidence of achlorhydria of less than 20 per cent, which is only about one-half of that found in the group of 100 diabetic persons investigated.

Their results appear to warrant the conclusion that gastric acidity tends to be low in diabetes. The clinical importance of this observation is that when diabetic persons show signs and symptoms that suggest conditions for the diagnosis of which gastric acidity is considered, the fact that diabetes, *per se*, may be responsible for low acidity must be considered. Their investigation did not concern cause and effect. That diabetes may be responsible for altered function of the gastrointestinal tract is suggestive. It is interesting to note that gastrointestinal disturbances are not uncommon in this disease, in the absence of the usual causes. Thus, in addition to achlorhydria, diarrhea may be noted occasionally and constipation commonly, and "cramps," vomiting or dilatation of the stomach may be observed prior to the onset of coma. Hypertrophy of the duodenal mucosa is also a suggestive sign; this characteristic was an almost constant observation at autopsies, in cases of diabetic coma, prior to the days of the use of insulin. This phase of the subject is now being investigated.

**TREATMENT.—Diet.**—The tendency in the treatment of diabetes during the year 1931 seems to be swinging towards the use of a moderately high carbohydrate diet and one rather low in fats. There are still, however, many

men who feel that the high carbohydrate diet (a diet of 250 to 350 grams of carbohydrate per day) is the ideal one. This group is composed mostly of observers in the West and on the Pacific Coast. While such a diet theoretically overcomes the dangers of a hypercholesteremia from a high fat content and while it actually makes the patient's diet a practically normal one, in that they can eat average amounts of high carbohydrate foods, it has the disadvantage that these patients must of necessity take rather large doses of insulin.

The observers in the middle West still feel that a low carbohydrate, high fat diet is the ideal one, not because it supplies the pancreas with less carbohydrates to utilize, but because these patients require less insulin than the average. It, however, has the disadvantage of being a very unpalatable diet and that theoretically, at least, the danger of developing acidosis from such a diet is increased. The majority of men particularly interested in diabetic work, use a diet in which the carbohydrates are moderately elevated—about 100 to 150 grams per day—with the fats proportionately decreased. All observers feel that diabetics should be on a low caloric diet and an allowance of 30 calories per kilogram per body weight per day seems to be the most satisfactory. There have been no outstanding developments in this particular phase of diabetes during the year of 1931, but rather a drifting toward the higher carbohydrate allowances.

There have been published during the last year many splendid reviews of large series of cases of diabetes which give considerable information about the present treatment and complications of diabetes.

E P Joslin (J A. M A 97 595 (Aug 29) 1931), in appraising the present treatment of diabetes, states that the average patient consulting him in January, 1931, had lived half again as long as those of 1921 and that he was 8 years older. He has noticed a decrease in the proportion of males—44 per cent in 1931 as contrasted with 55 per cent in 1911. He emphasized the fact that arteriosclerosis has taken the place of coma in diabetics as a cause of complication and death. As to the mortality, a growing number of patients now outlive their life expectancy and a leading insurance company acknowledges that since the discovery of insulin diabetic mortality has decreased in the young and that its increase in the old is largely to be explained not by an increase in the disease but, rather, because of an increase in the total number of diabetic patients. He feels that the diabetic in 1931 has 1 chance in 10 or possibly 1 in 5 of living longer with his diabetes than his neighbor of the same age without it. The question of hypercholesteremia and its relation to arteriosclerosis is still an unsolved one and radical changes from the routine standard diets developed through years of experience should be slowly made.

The writer speaks of the high carbohydrate and the low carbohydrate types of diet but prefers and uses a diet containing a moderate amount of carbohydrate (100 to 200 grams). The total calories for the day should be calculated to maintain the patient's weight about 10 per cent. below the ideal weight for his age and height. He stresses the importance of exercise and the futility of "pills" and other proprietary medicines as a substitute for insulin.

He points out the increasing danger of diabetic coma with increasing age

and the importance of adjusting the treatment accordingly. Joslin feels that the failure or unsuccessful treatment of diabetes in 1931 is due to inadequate facilities for laboratory study of the case or lack of education of the patient.

The avoidance of overnutrition, consequently overweight, is always a standard principle, but the reduction of excess weight must be accomplished in a gradual manner, according to Joslin (*loc cit*). The nutritional requirement is a factor to be taken into consideration when the calculated prescription is changed into food. If the basic prescription has been adequate and the food carefully chosen, considering the vitamin and mineral content, a diet can be devised which will adequately nourish the diabetic—but if this is not the case, it must be remembered that diabetics as a class, particularly if undernourished, are easy prey for the various results of malnutrition.

It is evident that tuberculosis is often associated with diabetes. There may be several reasons. One simple but logical one which has been advanced is that tuberculosis may be termed a disease of malnutrition to which underweight people are most susceptible. Thus, the diabetic who is undernourished must pay the penalty resulting from poor nutrition.

One gram of protein per kilogram of body weight will permit an adequate supply of protein of good quality, such as meat, eggs, fish, cheese and milk, which in turn will reinforce the mineral content. The amount of calcium and phosphorus already present is increased definitely by the inclusion of milk and whole grain cereals. With the frequent use of fruits and vegetables, the iron content may be increased to maintain the Sherman standard of 15 mg daily.

Peas and spinach have a high percentage of iron

In an analysis of the diet regarding the vitamin content, "A" will be provided for in the butter, milk, cream and vegetables, "C" through citrus fruits and vegetables, but in the case of "B," which is closely connected with the correct functioning of the digestive tract, careful selection must be made, as many diets are found to be inadequate in this respect. Whole grain cereals and milk will help to improve the intake of vitamin B.

**Insulin.**—Insulin has been in rather general use since 1923, and although there has been a tremendous amount of research done on its structure and action, there is as yet no satisfactory criterion for the gauging of the insulin dosage. Most of the clinicians particularly interested in diabetic treatment, have developed a rather arbitrary method of judging the initial insulin dosage, and increase or decrease this according to the patient's response. While these methods are fairly satisfactory they are far from scientifically correct, and any attempt to establish definitely the matter of dosage is welcome.

J. R. Williams (Ann Int Med 5:264 (Sept.) 1931) advances what he calls the "insulin coefficient" which, while far from ideal and not applicable in all cases, is of some value as a guide to the initial dose. His method of determining the coefficient is as follows:

The patient is placed on a standard diet (standard for the patient's weight and height) and continued on this diet until the amount of sugar in a 24-hour specimen remains constant. The amount of sugar in the urine is subtracted from the total amount in the diet, thus giving the amount of carbohydrate that can be

taken care of by the insulin manufactured by the patient's pancreas. This is then divided by 4 (Williams believes that 1 unit of insulin burns 4 grams of sugar) and this is called the "insulin coefficient." The total number of units is then subtracted from the total number estimated at 1 unit for 4 grams necessary to take care of the total carbohydrate of the diet, and this amount is administered in 24 hours.

A simpler way would be to calculate the total sugar excreted in 24 hours and divide by 4. Williams (*loc cit*) has found that readjustment of the time and frequency of meals, as well as the time and amount of insulin, are necessary for the full utilization of insulin. Reactions are a sign of wasted insulin, as is a subnormal blood sugar 2 to 3 hours after administration. He feels that the patient should be kept in that state of balance which will permit him to utilize to the fullest extent the insulin manufactured by his own pancreas. This method is presented as a help to control the insulin dosage and is particularly valuable in clinical research which must of necessity be done on the human. While it may not be possible to share Williams' enthusiasm over the "insulin coefficient," and while there are many cases in which the patient's response is not in accord with the 1 to 4 ratio, the method offers a safer basis for initial insulin dosage, particularly in those cases where it is impossible to follow with adequate blood studies.

The effect of *insulin shock* on the myocardium has been considered by 2 groups of writers, *ie*, W. S. Middleton and W. H. Oatwag, Jr. (Am. J. M. Sc 181:39 (Jan.) 1931). These observers point out that in the diabetic there exists an inability of the tissues to utilize glucose and a certain handicap



falls upon all tissues including the heart in the limitation of a readily available source of energy. In addition to this, there is in many cases of diabetes a tendency for the development of arteriosclerosis and an additional impediment to proper function of the myocardium as caused by impaired coronary circulation. To this already impaired cardiac mechanism insulin may add the theoretical chance of injury through hypoglycemia. This they have shown through experimental and clinical observations is a real hazard.

Electrocardiographic studies on 11 cases in shock showed change in the waves, particularly the T-wave, and evidence of change in conduction. They feel from their studies that extreme care should be used to prevent the development of hypoglycemia in cases of diabetes showing myocardial changes and also that, in any case, the intentional inducing of insulin shock is unphysiologic and, in view of possible myocardial injury, cannot be condoned if avoidable. A. E. Parsonnett and A. S. Hyman (*Ann. Int. Med.* 4: 1247 (Apr.) 1931) report 4 cases which developed typical attacks of coronary thrombosis proven by electrocardiography due to what was evidently insulin shock. Unfortunately, these cases were treated without adequate laboratory corroboration in most instances.

From the above mentioned abstracts it must be assumed that undue hesitation is not desirable in the use of insulin in all cases of diabetes in which it is indicated. But the lesson to be learned is that there must be hesitation about attempting to bring the blood sugar within absolutely normal limits in the elderly diabetic. A safe level at which to keep the fasting blood sugar is a number of milligrams per 100 c.c. equal

to the patient's age plus 100, so that in a patient of 55 years, efforts should be directed towards keeping the blood sugar at a level of 155 mg. per 100 c.c. This has been the custom of the writer for some few years and, as a result, in no case has any serious cardiac damage developed from hypoglycemia.

**Insulin Resistant Diabetes.**—Much has been published about insulin resistant diabetes and during the past year many cases of so-called "central diabetes" have been reported. The authors of these articles feel, because of the difficulty of controlling the case with the usual insulin dosage, that the disease is due to some lesion in the vicinity of the pituitary gland and undoubtedly there are many conditions which affect the brain-stem in the vicinity of the pituitary fossæ, producing hyperglycemia and glycosuria. However, in carefully analyzing these cases, the impression is obtained that adequate insulin has not been given to rule out the question of insufficient treatment.

Individuals vary in their reaction to insulin and as yet no satisfactory method has been developed for determining the exact dosage necessary in any particular case. It would seem, therefore, that many of these cases are simply cases in which the insulin administered has not been properly adjusted to the body requirements.

M. Labbé (*Rev. belge sc. méd.* 3: 465 (May) 1931) feels that most of these cases are false cases and he stresses particularly that those which show a true resistance to insulin should present the following 3 characteristics:

1. In a diabetic patient who is placed on a proper and definite regimen, insulin does not reduce either the glycosuria or the ketosis, contrary to usual conception of this mechanism.

2 To combat the glycosuria and acidosis and to maintain the equilibrium of nutrition, it is necessary to inject doses of insulin which are largely in excess in a diabetic patient who is on a proper regime

3 Insulin administration subcutaneously or intravenously in cases employed in the test of hypoglycemia does not reduce glycemia or reduce it less than would be observed in diabetic patients

It would seem a better therapeutic procedure from Labbé's work and from a careful analysis of the work reported in this country, to consider that such a condition as insulin resistant diabetes is a very, very rare occurrence and that, if possible, the time and size of the insulin doses should be adjusted to the individual case. A procedure of help in balancing the insulin dosage is an examination of the urine for quantitative sugar every hour, or a more accurate method the determining of the amount of blood sugar every 2 hours during the day and night. From these findings it is often possible to satisfactorily regulate the dosage of insulin to control the hyperglycemia.

A very interesting method has been devised for the investigation of the *functional reserve capacity of the pancreas*. This is described by R. N. Santos and F. Soutó (Endocrinology 15:107 (Mar-Apr) 1931), who have taken advantage of the fact that subcutaneous or intravenous injections of duodenal "secretin" will stimulate the islands of Langerhans and produce a fall in the blood sugar. They estimate that the reserve capacity of the pancreas may be stated quantitatively as 450 units of insulin. This is calculated by assuming that the average individual consumes a carbohydrate ration of 500 grams a day, which requires an approximation

of 250 units for its utilization. It has been shown that glucose tolerance of a normal individual is 0.85 grams per kilogram per hour, which for a man weighing 70 kilograms would be approximately 1400 grams of carbohydrate, requiring for their consumption the activity of 700 units of insulin. Considering that 1 unit of insulin burns 2 grams of carbohydrate, subtract from 700 thus obtained, the 250 which they estimate to be the daily amount used by the average individual, and they conclude that 450 units is the functional reserve capacity of the pancreas.

In doing these tests they inject secretin intravenously or subcutaneously and determine the fasting sugar level, and then determine the blood sugar values at intervals of 30 minutes for 2 hours. Santos and Soutó (*loc cit*) have been able to show that in certain cases of diabetes the secretin has been able to liberate an amount of insulin sufficient to reduce the blood sugar to normal for at least the period of observation, while in other cases there was no appreciable change even after 2 hours. They stated that the subjects that do not react to the secretin with hypoglycemia represent a very serious type of diabetes, and this has been borne out clinically. Other cases which appeared to be serious were shown to have lower reserve capacities than might be considered normal. While this test and the use of secretin is still a laboratory procedure only, it is an interesting field of speculation for the future.

**Various Methods of Treatment.**—Adjuncts in the treatment of diabetes have been many during the past few years and among those advocated to replace insulin in whole or part are **artichokes** as an article of food and certain **liver** preparations by mouth for

their effect in lowering of the blood sugar. Recent work has cast considerable doubt on the efficacy of either of these methods.

H B Stein, B B Longwell, and R C Lewis (Arch Int. Med. 48:313 (Aug) 1931) state that the carbohydrates of Jerusalem **artichokes** are absorbed and utilized by the diabetic patient as are an equal amount of carbohydrates from any other source. Wherever there has been an apparent benefit from the feeding of the artichoke, there has occurred the formation of large amounts of intestinal gas from fermentation and a reduction of the assimilable carbohydrates.

P C Brett, W. A. Broom and F O. Howitt (Lancet 1:20 (Jan 3) 1931) were unable to demonstrate any effect on the blood sugar in rabbits from the use of **liver extract** prepared either from fresh or frozen liver.

S Soski, H F. Binswanger and S Strouse (Am. J. M. Sc. 182:675 (Nov.) 1931) confirm the report of the lack of satisfactory evidence of the advantage of **liver** or **artichokes** in the diabetic regime in a series of carefully controlled experiments. While this work is not a contraindication to the use of artichokes in the diabetic diet, it would certainly be wise to calculate their carbohydrate content in the day's allowance.

**Treatment of Coma.**—A summary of the routine treatment of coma by various authorities gleaned from current literature is:

1 Application of **external heat**.

2 High compound **enema** to clean the bowels.

3 **Insulin**. The initial dose varies depending on the depth of coma, but ranges possibly from 40 to 90 units. This is repeated in half the quantity in

from 1 to 2 hours, depending on the patient's condition.

4 Forcing of **fluids** by mouth, vein, rectum or subcutaneously. In any case of actual or impending coma, **normal salt solution** given intravenously, 2000 to 6000 c c (2 to 6 quarts) more in 24 hours, has proven of great value, particularly in those cases developing anuria. None of these procedures are new, but it would seem from personal experience that the more often a routine method is followed in the handling of these cases, the better the results obtained.

In conjunction with the intravenous use of saline, it is of interest to read that R. Kuhn and L. Witscher (Klin. Wchnschr. 10:1616 (Aug 29) 1931) have found a definite change in the chloride metabolism. In all the more severe diabetic conditions they found a hypochloremia. It frequently precedes ketonuria, but when other symptoms have disappeared, it indicates a latent still threatening disturbance. In the most severe cases of diabetes mellitus a hypochloremia can be demonstrated and in the majority of these cases the authors found a hypochlorhydria or achlorhydria. These disturbances in the chloride metabolism indicate changes in tissue conditions which the authors term "rigid" chloride retention, and which they consider due to the hypofunctioning of the pancreas, a condition which intravenous use of normal saline will tend to overcome.

5 **Glucose** is given intravenously by many authorities both to help the ketosis and to prevent the patient from passing into hypoglycemic coma.

6 **Stimulants** are usually indicated and vary with the individual symptoms.

7 The use of soda by mouth, bowel, or vein seems to be falling into disuse.

In the treatment of coma Murphy and Moxon (*loc cit*) advocate the use of adequate insulin (40 to 50 units every 2 hours) to control the situation and the administration of larger quantities of fluids by mouth, vein or subcutaneously (normal saline 2000 to 4000 c c—2 to 4 quarts—or glucose solution) They did not administer alkali in any form to patients with coma

Coma and arteriosclerosis are the chief complications The former may be eradicated by educational measures plus insulin. The latter is one of the greatest problems in diabetic management and is the cause for the rising death rate among diabetics Insulin was necessary in one-third of the cases seen by Wendt and Peck (*loc cit*) They were able to maintain more nearly constant blood sugar level in some patients by feeding them every 8 hours and found that these cases required less insulin on such a regime

#### SURGERY IN DIABETICS.—

H. J. John (J Lab and Clin Med 16 775 (May) 1931) presents a careful statistical review of surgery of the pre- and post-insulin era. The mortality in 1728 cases of the first group was 31.3 per cent, while in 3676 cases (including 773 personal cases of the author) the mortality was 12 per cent. for the post-insulin era

He divided the cases of diabetes requiring surgery into those of *emergency* and those of *election*. In the *non-emergency cases* the routine preoperative management differs little from the routine of standardizing such a case without the surgical consideration. The author uses a diet consisting of at least 100 grams of carbohydrates, 60 to 80 grams of protein and a fat portion which varies with the desired caloric total. The use of insulin is, of course, de-

pendent upon the laboratory findings in the individual case The same diet is given postoperatively If oral feeding is contraindicated the glucose is given by vein with enough insulin to control the hyperglycemia

In *emergency operations* the amount of treatment given depends upon the acuteness of the surgical condition It is the author's custom to give 10 Gm (2½ drams) of glucose, as the 50 per cent solution, intravenously, immediately and with the same syringe withdraw blood for laboratory analysis If time or the surgical condition permits, more glucose is given with insulin, the amount depending upon the laboratory findings An effort is not made to "standardize" the patient, but rather to send him to the operation free from ketosis and with a slight carbohydrate excess

The author stresses the importance of close observation of the patient and of altering the treatment accordingly He also advises a blood culture if any infection is present If bacteremia is found and death should occur, it will not be a surgical one. A second blood culture should be taken 24 to 48 hours postoperatively in all cases of infection to ascertain whether bacteremia has developed.

After the operation the oxygen tank should be used in case of any degree of anoxemia, the clinical signs of which are excitability, headache, rapid pulse and dusky appearance of the nails He advocates the early use of oxygen rather than waiting for the development of cyanosis

E. W. Saunders (Ann. of Surg. 94: 161 (Aug) 1931) believes that the severity of infections in patients with diabetes is probably due to enhanced growth of glycophilic organism in tissue

abnormally high in dextrose and with a pH most favorable to toxin production. Ninety per cent of patients requiring surgery are over 50 years of age and are suffering from complications much more severe than the diabetes. Many of these surgical conditions are brought out by a complication of the disease. Maintaining a low blood sugar with a resultant low tissue sugar and change of tissue pH helps considerably in controlling the infection when surgery is attempted. He points out that gastric or duodenal ulcer, gastritis or duodenitis, or acute cholecystitis may cause edema of the pancreas, peripancreatitis or subacute pancreatitis. This not only causes an exacerbation of the diabetic condition, but also presents the clinical picture of a surgical lesion and might well explain the difficulty in differential diagnosis between impending coma and an acute, surgical condition of the abdomen.

F. A. Bothe (Pennsylvania M. J 34:624 (June) 1931), in presenting 150 consecutive cases of surgery in diabetics stresses the importance of **early operation** or at least early active treatment in *carbuncles*. In this series there were 8 carbuncles with 4 deaths, 50 per cent mortality. All 4 cases showed a positive blood stream culture of staphylococcus, and all 4 had been treated for at least 2 weeks before admission to the hospital. From his personal experience Bothe feels that infections in the diabetic are conditions of grave importance and the cases should be hospitalized if at all possible. He has also shown that cases of diabetes coming to the hospital after adequate treatment at home are much better surgical risks than those in which treatment has been inadequate or entirely absent. He stresses the point that glycosuria and hyperglycemia are no contraindications to surgery and feels

that patients can do better if there can be some excess of glycogen or carbohydrate in the body. The author feels that unless the surgeon is well versed in the diabetic treatment, the case might better be handled by a medical man with metabolic experience, both before and after operation, and that the time of operation should be decided upon on a basis of laboratory findings, rather than surgical judgment.

### DIABETES MELLITUS IN CHILDREN. —ETIOLOGY.—

**Heredity** is an undoubted etiologic factor in diabetes, according to Priscilla White (J. A. M. A. 95:1160 (Oct 18) 1930). Repeated questioning and the fact that diabetes may be latent in an adult member of the family and not appear until after it has occurred in the child, have increased the percentage of history of heredity in her juvenile diabetic patients. Whereas the fatal cases showed a history of heredity in 20 per cent, in the living cases this has steadily risen year by year until it has reached 40 per cent. P. J. Cammidge (Brit. M. J 2:738 (Oct 27) 1928) found that 28 per cent. of a group of 800 consecutive diabetic patients gave an ancestral or familial history of diabetes.

According to R. Priesel and R. Wagner (Klin. Wchnschr. 8:1398 (July 23) 1929), diabetes mellitus is inherited as a *recessive* as well as a *dominant* character. Cammidge has found from breeding experiments with mice that the natural high blood sugar is recessive to a normal blood sugar in the same way that albinism is recessive to color. He also believes that in human beings the diabetic tendency is transmitted in some cases as a dominant, in others as a recessive, Mendelian characteristic. As a *dominant* characteristic, it is transmitted

directly from diabetic patients to the child. As a *recessive* characteristic it may also be transmitted through healthy carriers, and persons manifesting the disease may not have a parent or grandparent similarly affected, although the disease probably will be found in some collateral relatives. Cammidge contends that diabetes is more likely to be grave and to appear earlier in each generation when transmitted as a recessive characteristic, and to be mild and to appear later when transmitted as a dominant characteristic. The dominant form tends to perpetuate itself and the recessive form tends to self extinction. According to M. Labbé (J. A. M. A. 97: 1087 (Oct 10) 1931), the rôle of the paternal is much greater than the maternal heredity, since the diabetic woman seldom has children.

**Obesity**, according to S. F. Adams (J. Nutrition 1: 339 (Mar) 1929) may be an important predisposing cause of diabetes in young persons, since more than 30 per cent of a group of diabetic patients less than 20 years of age were more than 20 per cent *overweight* before the onset of the disease. However, *overheight*, which is an almost constant characteristic of the prediabetic child, is thought to be a much more important factor than overweight in the cause of diabetes in children. According to White (*loc cit*) *overheight* in the child corresponds to *obesity* in the adult. Since the etiology of diabetes in the child is still a mystery, the possible combination must be considered of an hereditary taint and of an environment producing maximum growth. As White has pointed out, the cause of *overheight* can only be surmised. It may be the result of optimum nutrition or of infections with their subsequent gains in length. Overgrowth may be associated

with hyperactivity of other glands of internal secretion, particularly the pituitary.

There seems to be a close correlation between *age* and *growth* as predisposing causes of diabetes in childhood. The maximum incidence of juvenile diabetes mellitus in the thirteenth year are believed by Priesel and Wagner (*loc cit*) to indicate a close relationship between the number of available islets of the pancreas and growth. According to these authors, there is always a congenital deficiency of islets and the manifestation of latent diabetes is dependent primarily on the number of these available. Juvenile diabetes often is not actually progressive but only appears to be so.

**CHOLESTEROL**.—Considering 230 mgs per cent as the upper limit of normal, Priscilla White and Hazel Hunt (New England J. Med. 202: 607 (Mar. 27) 1930) have concluded that excess of cholesterol of the blood is an exception in uncomplicated diabetes in children. Cholesterol, according to these authors, is a measure of total lipoids. There is no close correspondence between glycosuria and blood sugar, on the one hand, and cholesterol, on the other. The duration of the disease in the child, as in the adult, is without significance as regards the cholesterol. Age is a factor which increases cholesterol since it rises during the age period between 15 and 19 years. Eventually, even with advancing age and duration, there is a subsequent tendency for the cholesterol to decline in amount. Complications of diabetes, such as *arteriosclerosis*, *coma* and *tuberculosis*, occur both among children with high and low percentage of cholesterol. Over-nutrition was found to be accompanied by an increase of cholesterol. Extremes in variation



above or below the normal body standard in weight are accompanied, as a rule, by excess of cholesterol, but abnormalities in stature were without influence. Although acidosis of slight degree is not regularly accompanied by an increase of cholesterol in the blood, when acidosis reaches the stage of diabetic coma there is always an increase of it. In diabetes of decreasing severity the average cholesterol value is 20 per cent lower than in cases of progressive diabetes; in mild diabetes its value is 10 per cent lower than in severe cases.

**BASAL METABOLISM.**—As a result of metabolism studies in 7 diabetic children, Beck (Monatschr. f. Kinderh. 48:256, 1930) observed that in the acute stage of the disease the basal metabolism was always definitely increased. Following the administration of insulin, however, the rate decreased. Each exacerbation of diabetes was accompanied by an increase. In *infections* accompanied by fever, the basal metabolism was greatly increased, appearing before the elevation of temperature began and lasting a long time after it had disappeared.

**PHYSICAL DEFECTS.**—R. Priesel and B. Wagner (Ztschr. f. Kinderh. 49:419, 1930) carefully examined 107 diabetic children and recorded the defects which consisted of such abnormalities or pathologic conditions as *gigantism*, *dwarfism*, *imbecility*, *curvature of the little finger*, *nodule of the ear*, *lordosis*, etc. The authors state that stigmas which occur in diabetic children are not discovered until an exact examination is made for the slightest deviation from the normal.

**CAUSE OF DEATH.**—The 3 possible causes of death in cases of uncomplicated diabetic coma advanced by E. C. Dodds and J. D. Robertson (Lancet

1:852 (Apr. 19) 1930) are: (1) advancing coma, *ie*, acidosis or ketosis according to the theory supported; (2) nitrogen retention, (3) circulatory failure.

This study of (a) the aceto-acetic acid, and (b) the alkali reserve content of the blood in patients in diabetic coma failed to support the theories that ketosis and acidosis were causes of death. In many cases of noncomatose diabetic patients the blood was found to have a higher aceto-acetic acid content than in the comatose patient and furthermore, upon recovery from coma it was found that it rose. In the fatal cases it was found that death was preceded by a persistently falling blood-pressure, indicating the importance of circulatory failure as the cause of fatal termination.

**PROGNOSIS.**—Early recognition and adequate treatment of juvenile diabetes, according to B. D. Bowen (J. A. M. A. 95:565 (Aug. 23) 1930), are the most important factors in obtaining good results. Before the discovery of insulin, diabetes in children was almost invariably fatal. Insulin has changed the prognosis completely. F. N. Allan and R. M. Wilder (J. A. M. A. 94:147 (Jan. 18) 1930) report that 32 children with diabetes were seen at The Mayo Clinic 3 years before the introduction of insulin. One was admitted moribund from coma; 28 received training in dietary management; 9 of the latter survived to benefit by insulin. Two have not been traced. The deaths of all others have been reported. Of 167 children treated at The Mayo Clinic in the past 6 years after the introduction of insulin, 17 have died; only 1 child died at the Clinic, being moribund from diabetic coma upon admission. An analysis of the fatal cases revealed that, with possibly 2 or 3 exceptions, death

occurred from preventable causes. The authors conclude that now, with insulin available to insure control of diabetes, deaths from coma should not occur even in severe diabetes.

Priscilla White (*loc cit*) points out that at the onset of the disease the diabetic child is characterized by precocity. His physical and x-ray ages are 18 months and his mental age 8 months in advance of his chronologic age. However, after years of duration of the disease, there may be some evidence that physical growth has been retarded. H. A. Harris (*Brit. M. J.* 1:700 (Apr. 25) 1931) states that x-ray examination of the long bones at stated intervals is a valuable means of recording the repeated arrests of growth in children suffering from metabolic disease such as diabetes. The lines of the arrested growth tend to persist in those bones which are close to joints having essentially monaxial movements such as the ankle and knee. Yet, even when there has been some late evidence of retarded growth, the stature of the child, according to White, does not fall appreciably below the standard average, and his mental growth continues above the normal average. Although it is known that the *complications* associated with diabetes in the adult can occur in the child, it is the diabetic child treated with inadequate methods of yesterday who develops cataracts and arteriosclerosis. In contrast with the adult, the insulin-treated diabetic child, according to Bowen, does not seem to have an impression of *fatigue* following normal, physical effort.

**TREATMENT.**—The adequate treatment of the diabetic child is a most difficult problem and tests the skill of any physician. The difficulty lies not so much in the severity of the disease,

as in the 4 variables that exist. Of these, the first is the reliability or non-reliability of the child, second is the emotional stability, third the variability of exercise, and fourth the inevitability of intercurrent infections (Priscilla White *loc cit*). Every case of juvenile diabetes, according to F. N. Allan and R. M. Wilder (*loc cit*) should be considered as potentially severe and careful dietary management should be instituted, even when glycosuria and hyperglycemia disappear promptly at the beginning of treatment.

**Dietary.**—Adequate treatment, Priscilla White (*loc. cit*) believes, implies a diet, first, in which the caloric value is such that growth and development neither exceeding nor falling below normal will occur, and secondly, in which the proportion of carbohydrate, protein and fat is so adjusted that after years of treatment it will neither produce injurious effect on the various body systems nor increase the severity of the disease. It may be true, and probably is true, that several possible dietetic combinations of carbohydrates, protein and fat will answer these requirements.

Bone growth, as is pointed out by N. B. Foster (*J. A. M. A.* 94:1971 (June 21) 1930), requires lime. Milk, therefore, is necessary in the ration of the healthy child. A quart of milk can easily be made a part of the daily diet of the child since, with the use of insulin, the milk sugar causes no obstacles. From the point of view of mineral and vitamin requisites, raw fruits and green vegetables must also be included. Fruit juices, tomato juice, leafy vegetables, carrots, fats (such as butter and cod-liver oil), each furnish some element essential either to growth or to health. The protein requisites are also greater during the period of growth.

While 1 gram of protein per kilogram of body weight may be sufficient for the majority of adults, 2 grams is not too much for the growing child, and some children thrive best on even larger quantities

In general, the diet outlined by F N Allan and R. M Wilder (*loc cit*) contains for each diabetic child not more than 50 grams of protein; carbohydrate is moderately restricted, and fat is depended on as the main source of calories. The caloric requirement is estimated as accurately as possible to provide adequate nutrition, and exact attention is paid to the supply of vitamins and minerals. With few exceptions, growth and development have proceeded normally in their patients, and in the case of the girls, menstruation usually has been normal after they reached puberty.

White (*loc cit*) recommends a diet in which the prescribed caloric value is at least 50 per cent above the basal metabolism and one in which at least 25 per cent of the total calories are in the form of carbohydrate, thus presupposing the use of insulin, and from 10 to 15 per cent in the form of protein. According to this author, the former advocates of high fat and high caloric diets report normal rates of growth in diabetic children but state that the disease becomes increasingly severe. Individual interpretation of data, however, must be considered, as there are no established rules for measuring gains or losses of tolerance. A full decade of time will be necessary to tell which combination of diet will best answer all the requirements during the course of years. Until further evidence is available, it is far safer not to go to extremes; neither to adopt the low carbohydrate-high fat diet which appears to lower the

tolerance for carbohydrates, nor to adopt the reverse diet, which fails to protect and spare the pancreas which is diseased.

In dietaries for diabetic children, H A Rohrbach (Pennsylvania M J. 34:368 (Mar) 1931) considers an increased carbohydrate intake is of value, as there is an increased energy requirement for muscular activity, also the diet is more palatable and easily maintained. The protein requirement, as mentioned, averages from 2 to 3 grams per kilogram of body weight, to meet the demands of growth and tissue building. In this case, particularly, every allowance in diet for this vitamin and mineral content should be given, and in order to have liberal protection, 1 pint of milk, 2 eggs, at least 200 grams of a green, leafy vegetable, and 200 grams of fruit should be included in the daily diet.

It is evident in planning a diet, particularly in the case of diabetes with its various restrictions, that due consideration must be paid to all the normal nutritional requirements, as these remain, as a rule, essentially the same, unaffected by the disease.

**Insulin.**—Allan and Wilder (*loc cit.*) prescribe insulin in small dosage in almost all juvenile cases of diabetes, even when it is not needed to control glycosuria. This procedure may possibly check the progress of the disease and in any case, it permits immediate control, should failure in tolerance occur.

The parents must be trained to maintain a balance between the dosage of insulin and the diet, increasing the dosage of insulin on the appearance of glycosuria, and decreasing the dosage on the occurrence of symptoms of hypoglycemia. Even if insulin is not given, at least the parents should be trained to

inject it on the appearance of glycosuria. The urine should be tested for sugar every morning and every night so that a decrease in tolerance can be recognized and can be combatted without delay by an increase in dosage of insulin. Each new supply of Benedict's qualitative sugar determination solution should be tested by boiling 5 c.c. of the solution with a drop of corn sugar or honey. A solution that does not change in color when tested in this manner is not dependable.

There are certain cases of severe diabetes which are extremely difficult to control; those which require large doses of insulin 3 or 4 times a day and in which the patients pass rapidly into a state of acidosis if an injection is missed or the dose is inadequate. Even these patients respond satisfactorily, as a rule, if sufficient insulin is given. Since the disturbance is often only temporary, it is of greatest importance to use the amount of insulin required, however great that might be.

During *sickness* special precaution must be observed by making test of the urine at least 4 times a day, and increasing the dosage of insulin sufficiently to check the glycosuria. Even if the patient is unable to eat, insulin should not be omitted without medical advice, unless the urine is sugar free. With the appearance of *acidosis* insulin should be used in moderate doses frequently repeated, making a test of the urine or blood before each injection. Carbohydrate tolerance is lowered by *infections* of all kinds and degrees. In their presence, according to Gladys L. Boyd (Canad M A J. 21:520 (Nov.) 1929) either less food or more insulin should be given. Insulin must on no account be discontinued. Empirically, the author instructs the mother to leave

the insulin unaltered but to decrease the diet to two-thirds of its normal value. Such a measure enables the patients successfully to handle mild infections without any permanent decrease in the carbohydrate tolerance and without the development of acidosis. If the child is too ill to take food, carbohydrate must be given parenterally.

**Exercise.**—F. Hamburger (Munch med Wchnschr 76 1329 (Aug 9) 1929) called attention to the importance of muscular exercise for patients with diabetes. Diabetic patients excrete more dextrose at rest than when they take a moderate amount of exercise. The patients feel better on the days on which they are active. Parents should be instructed that there is danger of hypoglycemia if exercise is taken after an administration of insulin.

**Summer Camp.**—According to L. F. C. Wendt and F. B. Peck (J. Michigan M Soc J. 29:430 (June) 1930, J. A M A. 96:1217 (Apr. 11) 1931), every large community should have a camp for diabetic children. The aim of the camp is to get the child out of doors for a time and away from the parents, who may need a respite from the constant watchfulness so necessary in the treatment of their diabetic children. The child is also entitled to a vacation such as is given to other more fortunate children. The camp also tends to combat the development of abnormalities of personality due to overemphasis of the disease. Thirteen of a group of 31 patients at a summer camp, reported by Wendt and Peck, were able to have the insulin doses decreased.

**TREATMENT OF DIABETIC COMA.**—The metabolism, according to Gladys Boyd (*loc cit*), should be spared by putting the patient to bed and by relieving him of all possible exertion.

**Local heat** should be carefully applied. Adequate **fluids** must be given, as all patients are dehydrated. For obvious reasons, during the first 24 hours the bulk of the fluids must be given parenterally. Furthermore, the metabolism must be "converted to a carbohydrate one." This is usually accomplished with ease in the underweight child, but becomes increasingly more difficult for each pound of excessive fat that has accumulated. Five per cent glucose in normal saline may be given subcutaneously and repeated every 4 to 6 hours, or in more urgent cases 10 per cent glucose solution may be given intravenously, it is seldom necessary to repeat the intravenous therapy. Since circulatory failure is often a contributory cause of death in diabetic coma, fluids should be administered very slowly intravenously, in a total quantity of not more than 10 c c per pound of body weight. Immediately after the intravenous injection of glucose, **normal saline** should be given. **Chlorides** must be administered in sufficient amounts to make up for the depletion usually present, otherwise overzealous administration of carbohydrate and neglect of the chlorides may save the patient from an *acidosis* only to give him an *alkalosis*. When improvement permits it, small quantities of **orange juice** or of **glucose** are given *per os* at frequent intervals and the parenteral administration discontinued as soon as sufficient quantity of fluid and carbohydrates can be administered in this manner.

It, of course, would be impossible either to convert the metabolism to a carbohydrate one or to rid the body of its excessive fatty acids without **insulin**. The efficiency of insulin therapy depends directly upon its early administration. If there is unavoidable delay before the

patient can be admitted to the hospital, 40 to 50 units of insulin may be given at once with great advantage. The first dose of insulin may be given intravenously with the glucose in those patients in whom the depth of the coma or the duration of the symptoms make rapid action imperative. In such cases 2 units of insulin may be given with each gram (15 grains) of glucose. In those cases requiring less urgent treatment, insulin in the proportion of 1 unit for each gram of glucose may be given by the hypodermic method whenever the subcutaneous injection of glucose is made. After the return to an adequate intake of fluid and carbohydrate by mouth, small doses of insulin (10 to 15 units) may be given every 4 hours, until the patient becomes sugar-free, or his condition warrants placing him on a diet with small amounts of insulin before meals. It is not advisable to keep the patient aglycosuric until he is fully conscious, because of the danger of hypoglycemia.

Boyd recommends **gastric lavage** with **soda bicarbonate solution** for *vomiting and distention of the stomach* persisting after the general treatment. *Constipation*, which is usually marked, should be treated by **high colonic irrigations**. In case of *circulatory failure*, **digitalin** every 4 hours, or, in severe cases, digitalin alternated every 2 hours with **caffeine sodium benzoate** seems of value. *Bicarbonates* are seldom indicated, although occasionally in a few cases where progress appears slower than anticipated, a few small doses of **soda bicarbonate** by mouth has hastened recovery.

**DIAPHRAGM.—MORBID ANATOMY.**—While the physiology has been much discussed, the pathology

of the diaphragm has been neglected, according to B Lucké (*Ann Int Med* 5:750 (Dec) 1931), even though a thorough knowledge of morbid structure is a necessary prerequisite to an understanding of the functional diseases.

But few diseased processes affect the diaphragm as primary lesions, but secondary lesions are unusually common, spreading from adjacent organs and tissues in intimate contact with it, as the pericardium, the pleuræ, the peritoneum, the gall-bladder, liver, stomach, spleen, adrenals, kidneys, pancreas and duodenum.

Primary neoplasms of the diaphragm are rare, less than a score have been reported in the literature, all being of the connective tissue series; fibromas, chondromas, lipomas and sarcomas. Secondary tumors are not uncommon. Lucké observed 18 secondary tumors among 164 pathological diaphragms. The growths were carcinomas in 14 and sarcomas in 3 cases, and the remaining tumor was a renal hypernephroma. In some cancers arising in the stomach, liver and gall-bladder, it may be difficult to determine whether the tumors had spread to the diaphragm by direct extension or by metastasis. Since the majority of the tumors found primary origin in abdominal organs adjacent to the diaphragm, the peritoneal surface was generally more heavily infiltrated than the pleural surface. Tuberculosis of the diaphragm is nearly always secondary to some focus elsewhere.

Lucké, in the course of his extensive studies, found 35 cases showing tuberculous lesions of the diaphragm in the 164 examined. The peritoneal surface was more often involved than the pleural surface, even when the primary focus was in the lung or the pleura. Acute inflammatory reaction, as diaphragmatic

pleurisy and peritonitis, are frequently found clinically.

Twenty-five instances of diaphragmitis were found in the series studied and there was not only an inflammation of one or both surfaces, but in every instance the muscles showed definite changes. In some, these were chiefly degenerative lesions and in others there was a true myositis. Degenerated muscle fibers were separated by an edematous fluid containing polymorphonuclear leukocytes and occasionally mononuclear histiocytes. Capillaries were found to be engorged, and the lymph channels prominently distended.

Inflammatory lesions of the diaphragm are no doubt of great clinical importance, and while Rohrer believed that lesions occurred in every case of pneumonia, Lucké was not able to share his opinion, since the latter found many cases of pneumonia without lesions of inflammatory, as contrasted with purely degenerative, character in the diaphragm. Lesions of the diaphragm, acute in nature may be followed by organization of exudate covering the serous surfaces and forming adhesions as well as the occurrence of patches of fibrosis throughout the muscles.

The degenerations found most frequently in the diaphragm were vascular degeneration, cloudy swelling, Zenker's hyaline degeneration and fatty degeneration. This investigator concludes that the efficiency of the diaphragm depends above all, on the ability of its component muscles to contract properly, and where tumors or tuberculosis or diaphragmitis and degenerations are found, he assumes that the functional powers of the muscle as a whole are considerably impaired, since these disease processes are followed by loss of contractile ability. This loss must of



necessity have serious consequences when the respiratory or circulatory mechanism is at fault

### DIARRHEAL DISEASES IN INFANCY.—ETIOLOGY AND PATHOLOGY.

—The relationship between diarrhea, tetany, fat digestion and calcium retention was studied in 3 patients by G Linder and C F. Harris (Quart J Med 23 195 (Jan) 1930) It was thought that the tetany of these patients was due to the calcium deficiency In 1 patient decalcification of the bones was so marked that spontaneous fractures occurred The possibilities accounting for the calcium deficiency were (1) an abnormal excretion of salts accompanying the diarrhea, or (2) the result of a high fat intake with disturbance of its digestion which inhibited calcium absorption, or (3) a failure of calcium retention due to a lack of vitamin D Most of the evidence favored the last theory, with possibly a minor rôle played by the others Treatment with ergosterol and by a limitation of fat intake in the diet was the suggested therapy

Infants with diarrhea often lose large amounts of fixed base but retain fixed acid in the blood, this resulting in acidosis A group of 25 infants with diarrhea of various degrees of severity was compared with a control group of 20 normal infants by L E Holt, Jr (Am J. Dis Child 39:1346 (June) 1930) in regard to their acid-base balance The loss of fixed base occurred chiefly by elimination through the intestines, partly by way of the alkaline intestinal secretions Treatment with solutions containing various salts, was in itself inadequate to combat the acidosis.

If infants who are dehydrated and have a decreased urinary output are

given an abundance of fluids, the excretion of acid through the urine will relieve the condition of acidosis This is the conclusion reached by L. A Hoag and E Marples (Am J Dis Child 42:291 (Aug) 1931) from an exhaustive study of the acid-base balance of 14 infants suffering from diarrhea and dehydration These patients were given large amounts of saline solution parenterally and the treatment did not lead to an abnormal accumulation of chloride nor to an increase of the loss of fixed base but did aid in the elimination of acids.

Certain instances in which an alkalosis has resulted from chronic diarrhea of infants have been observed by M. Maizels and C. B. McArthur (Quart. J. Med. 23 171 (Jan) 1930) An alkalosis is known to occur in infants who have been vomiting frequently with a resulting loss of acid Chronic diarrhea may also cause an alkalosis of the blood and 7 infants with this condition were noted. In both of these types of disease the urine sometimes is acid in reaction, due probably to a lesion of the kidney which interferes with the secretion of base The reason for this conclusion was the finding of a high plasma phosphate in the blood of 3 patients and an amount of titratable acid greater than ammonia combined acid, which suggested that most of the acid radicals of the blood were not in combination with ammonia, but with fixed base. The osmotic pressure of the blood was greater than normal in these patients with alkalosis

**DIETARY TREATMENT.**—The pulp of ripe apples has been recommended for the treatment of diarrhea in infants by E Moro (Klin. Wchnschr. 8:2414 (Dec. 24) 1929). A daily amount of 500 to 1500 Gm. (1 to 3

pounds) of the pulp was given with some variation according to age. A group of 52 children of 1 to 10 years of age suffering from various kinds of gastrointestinal disease, including dysentery and typhoid fever received this diet with occasionally the addition of **weak tea** to furnish additional fluid. Clinical improvement was noted in the majority of instances after 2 days of such treatment. Additions to the diet were made gradually, reserving milk and vegetables until the last. The advantages of the apple pulp were thought to lie in its tannic acid content and to the action of the pulp as an absorbent. It furnished a nonirritating bulk for the intestinal tract.

Employing the apple diet, S. Wolff (Deutsche med Wchnschr 56 2211 (Dec. 26) 1930) has had considerable success with the treatment of 150 patients suffering with diarrhea of various types. In several instances, the diet was continued for more than the customary 2 days without any harmful results.

A fruit diet for older children with acute intestinal disturbances was recommended by G. Fanconi (Deutsche med Wchnschr 56 1949 (Nov 14) 1930). **Fruit juices** alone may be given or together with the **pulp of apples and bananas**. After a day or two of such a diet, the condition of the intestinal tract usually improved. Later, other foods were added gradually, beginning with mashed vegetables, buttermilk and nuts, giving milk and cereals last of all.

Sufficient liquid with enough salt to permit water retention and provide enough calories to prevent inanition, are primary essentials in diet for an infant suffering from diarrhea. Arrest of weight loss should be attained by any diet that is prescribed. Mother's milk may be an excellent reparative type of

diet, but it is not a satisfactory "transition diet" to stop the diarrhea, therefore, L. Moll (Rev franç de pédiat 6 177, 1930) recommends a preparation of **milk of almonds and whey**. This preparation is especially well-fitted for younger nurslings. For older children, the author suggests a pudding made of a special flour with water, sugar, salt, egg and sodium carbonate, which is steamed, strained and diluted with tea, whey, milk of almonds or mother's milk. The almond milk diet is somewhat richer in calories and may be given from 4 to 5 days, even for 2 weeks, without exposing the child to danger from lack of protein or mineral substances. The average duration of the diet should be 1 week, after which the child's ordinary food may be given.

**DIPHTHERIA.—INCIDENCE AND MORTALITY.**—In the United States the diphtheria mortality rate during 1929 was the lowest ever tabulated. Statistics available from reports of Boards of Health of 78 cities (J. A. M. A 94.1838 (June 7) 1930) indicated a continuous decline in the number of deaths from this disease since 1923, with the exception of a slight rise in 1927, when a moderately severe epidemic of diphtheria swept over North America and Europe. In 1928, there were 3982 deaths from this illness in 78 of the largest cities in all parts of this country, a mortality rate of 13.25 per 100,000 population. In 1929, the deaths were 2682 or 7.73 per 100,000 persons and the cities having the relatively highest mortality rate were located in the East North Central area, which includes the states of Ohio, Michigan, Indiana, Illinois and Wisconsin. The rate was lowest in the cities of the mountain and Pacific districts.

During the year 1930 there was a still greater decline. In a total of 88 cities the rate dropped from 7.82 to 5.12 deaths per 100,000 population. The mortality from diphtheria in the cities continued to be lowest in the western mountain and Pacific states, although 2 other districts were very low also, *viz*, the south Atlantic cities located in Maryland, New Jersey, Virginia, Georgia, Florida and the District of Columbia, and in the territory including Minnesota, Kansas, Missouri, Nebraska (J. A. M. A. 96:1768 (May 23) 1931). Certain foreign countries, however, have experienced rather severe epidemics in the last few years. In Germany, for instance, the number of patients who have contracted diphtheria has increased each year since 1923. Burgers reported recently that over 38,000 persons had contracted it in Germany during the first 10 months of 1930, as compared with 19,599 instances during the entire year of 1923 (Berlin Correspondent J. A. M. A. 96:960 (Mar 21) 1931).

The reason for the reduction in the incidence and mortality rates of diphtheria in the United States has been attributed in part to the inauguration during the last several years of extensive campaigns urging immunization. An example of a very effective and rather unique plan for the immunization of large numbers of children is one instituted by the Board of Health of Detroit, and described by L. A. Geib and H. F. Vaughan (J. A. M. A. 97:366 (Aug 8) 1931). Beginning with 1928, all the free clinics for such immunization were abandoned and the work turned over to private physicians, while the activities of the Public Health Department were directed towards (1) postgraduate conferences in communicable diseases, (2) visits to physicians,

(3) popular health instruction to the public, and (4) home visits and parental instruction. A definite fee which the physician was to charge was established at \$1.00 for the Schick test and reading, and \$1.00 for each injection, or a total of \$4.00. If the patient was unable to pay, the health department reimbursed the physician to the extent of \$2.50. Toxin-antitoxin or toxoid was made available to physicians by the department, while in return the physician was asked to notify the Health Department of each treatment and Schick test done. The total expense, including the cost of the material, the payment of the physicians, the educational campaign, and the salaries of the cooperating nursing personnel was estimated at \$250,000 for a year, which was considerably less than the cost of medical care for the usual number of diphtheria patients. Since the inauguration of this plan about 80 per cent of the children of school age and about 70 per cent of pre-school children had been reached. The incidence of diphtheria in the city dropped to about one-fourth of that of preceding years.

**PATHOLOGY.**—The effect of diphtheria toxin on carbohydrate metabolism was studied by F. F. Schwentker and W. W. Noel (Bull. Johns Hopkins Hosp. 46:259 (Apr.) 1930). During the early stage of the toxemia produced in animals by injections of lethal doses of diphtheria toxin, the blood sugar first rose and then as the toxemia continued, the sugar fell to low levels. The preliminary increase in blood sugar apparently came from the liver and tissues which discharged their glycogen. When this supply was exhausted the blood sugar level fell. Late in the toxemia, however, a secondary rise occurred and was attributed to a suppression of in-

sulin production and a failure of the tissues to utilize the carbohydrate. Injections of insulin aided in the utilization of the sugar.

**COMPLICATIONS.**—The severity of diphtheria infections is known to vary considerably in different epidemics, that of 1927, for instance, being unusually virulent. In a survey of 100 patients with very severe diphtheritic infections, E. B. Shaw and H. E. Thelander (Arch. Pediat. 47:178 (Mar.) 1930) concluded that the virulence of the microorganism was responsible for severe infections in only 6 instances of this series, while a failure to make the proper diagnosis and to institute early treatment accounted for 92 of the severe infections. In 12 patients diphtheria occurred as a complicating illness of another disease and was consequently overlooked until it had progressed to an advanced stage.

The same warning in regard to delayed diagnosis and the postponement of the administration of antitoxin has been voiced by J. Greengard (Arch. Pediat. 46:441 (July) 1929). Among 726 instances of diphtheria admitted to a large contagious hospital there was a mortality of 16 per cent, the principal cause of death being cardiac failure, and the author considered the contributing factor a neglect in administering antitoxin early in the course of the infection.

The high incidence of *cardiac failure* among patients dying with diphtheria has stimulated several recent investigations. F. F. Schwentker and W. W. Noel (Bull. Johns Hopkins Hosp. 45:276 (Nov.) 1929) analyzed the findings of 39 such patients. The clinical symptoms could be divided into those which occurred early in the diphtheritic infection between the second to ninth day and those which occurred later, on the

seventh to fifteenth day of the disease. The symptoms of these two classes differed considerably and were based on 2 different pathologic conditions. The early failing hearts were thought to be severely injured by the diphtheritic toxin, while the late changes were due to inflammation which accompanied regeneration and repair.

A somewhat similar classification of *cardiac symptoms* was made by C. F. Brockington (Lancet 1:1387 (June 27) 1931), but late heart failure he attributes to a fall in blood-pressure. In the observation of a number of patients with faucial diphtheria, it was noted that, in the absence of an initial heart failure, the blood-pressure remained about normal for the first 7 to 9 days of the infection and then declined for 3 or 4 days, the lowest point being reached on the eighth to twelfth day of the disease. Recovery usually occurred by the twelfth to twenty-second day. If a patient with a severe diphtheria infection survives the first few weeks of his illness, he may succumb during the second or third week from severe circulatory collapse. The author attributed 50 per cent of deaths in the later weeks to this condition.

In an electrocardiographic study of 50 children between the ages of 5 and 14 years, suffering from diphtheritic infections of various degrees of virulence, C. Shookhoff and L. M. Taran (Am. J. Dis. Child 42:811 (Oct.) 1931) came to the conclusion that the myocardium was the portion of the heart which was primarily involved. Only 11 children of this series had any *clinical* evidence of *myocardial involvement* but the electrocardiograph demonstrated the lesion in a much larger number of patients. There was a similarity in the myocardial disturbances produced by diph-

theria, scarlet fever and rheumatic fever. However, in diphtheria, auriculoventricular conduction was normal throughout, which is not true in severe rheumatic heart disease. The average cardiac rate was higher in children with diphtheria than in those with scarlet fever. There were 16 per cent of this series of diphtheria patients who had a slurring of the descending portion of the QRS tracing, 60 per cent had an abnormal R-T transition, 36 per cent had changes of the T waves in the first 2 leads, and in 18 per cent there was a deviation of the axis to right or left.

A statistical study of the relationship between heart-block and diphtheria was conducted by S. Butler and S. A. Levine (Am Heart J 5:592 (June) 1930). Among 20 patients with heart-block of undetermined etiology, *i.e.*, not due to any evident arteriosclerosis, rheumatic fever and the like, one-half of the number, or 50 per cent, had a history of a previous attack of diphtheria. In 600 other patients, previous diphtheria had occurred in only 6 per cent. This marked difference in the incidence of diphtheria in the 2 groups was thought to be of some significance in regard to the etiology of heart-block.

Several instances of the more rare complications of diphtheria have been recorded lately. From 2 sources come reports of *hemiplegia* following diphtheritic infections. O. Saxl (Med. Klin. 26:307 (Feb 28) 1930) observed a patient, 8 years of age, who developed symptoms of *myocarditis* followed by a hemiplegia 3 weeks after the onset of diphtheria. In addition there was *cranial nerve involvement*, especially of the facial and hypoglossal. Recovery from the hemiplegia occurred slowly with a residual spasticity of one leg several months later. Hemorrhage,

thrombosis or embolism of a cerebral vessel have been suggested as etiologic factors in this complication but Saxl favors the last. C. Worster-Drought and I. M. Allen (Proc Roy Soc. Med 22:640 (Mar) 1929) reported a similar complication in a patient of 9 years of age.

An instance of *diphtheria of the penis*, not associated with a circumcision wound, was noted by A. L. Hoyne and A. J. Levy (J A M A 94:1395 (May 3) 1930). In the opinion of the authors, this is the first such complication of diphtheria reported. A boy of 7 years, who had been circumcised in infancy, developed a severe diphtheritic oral infection and very soon after, the remains of the prepuce became inflamed, edematous and covered with a thick yellowish exudate extending over the corona of the glans. Cultures of this exudate were positive for diphtheria bacilli.

Another unusual complication consisting of a *membranous infection of the umbilicus* of a 41-day old infant was described by J. C. Montgomery (Am J Dis Child 40:968 (Nov.) 1930). A slight infection of the umbilicus had remained after the cord sloughed. At the age of 3 weeks the infant began to have redness about the umbilicus and a grayish membrane developed with a small hard mass just beneath. Cultures showed diphtheria bacilli. The child developed paralysis of the legs and diaphragm and died of cardiac failure. Necropsy revealed degeneration of the myocardium as well as of the kidney and liver parenchyma.

D. Mortiz (Nourrisson 18:310 (Sept.) 1930) observed an infant, aged 18 months, who contracted diphtheritic meningitis, probably an extension of a middle ear infection of the same etiol-

ogy The diphtheria bacillus was found in the spinal fluid and after the infant's death in the grayish exudate at the base of the brain

#### DIFFERENTIAL DIAGNOSIS.

The difficulties of differentiation between simple "croup" and true laryngeal diphtheria led D M Tolle (Am J Dis Child 39 954 (May) 1930) to review signs and symptoms of 344 such patients By direct laryngoscopy, 61.6 per cent were diagnosed as true laryngeal diphtheria because of the presence of a membrane which was found to contain diphtheria bacilli on culture Symptoms similar to those of laryngeal diphtheria were produced by simple catarrhal inflammation of the larynx Of 18 such patients, 16 harbored other microorganisms, such as varieties of streptococci, staphylococci and pneumococci. In 5 other patients, the thymus was found to be enlarged on x-ray examination, 4 had bronchopneumonia, and 6 had severe nasopharyngeal infections, 22 had severe tracheobronchitis, 2 had foreign bodies, 3 had retropharyngeal abscesses, and 1 a laryngeal polyp

In a similar series of 66 patients suffering from "croup," W L Bradford and A D Leahy (Am. J. Dis Child. 40.298 (Aug) 1930) found that 38 had positive diphtheria bacilli cultures, and in 31 patients a membrane could be seen in the trachea by means of a laryngoscope. In 28 such children, no laryngeal membrane was seen and bacteriologic cultures contained no Klebs-Loeffler bacilli The microorganism which was predominant in the latter series was *Streptococcus viridans*, while in rarer instances there were strains of staphylococci, pneumococci and *Micrococcus cattarrhalis*.

**TREATMENT.**—For the treatment of virulent diphtheritic infections, espe-

cially during severe epidemics, large doses of concentrated antitoxin have been employed V Bie (Ugesk f laeger 92 55 (Jan 16) 1930, J A M A 94 902 (Mar 22) 1930) used a serum containing 700 antitoxin units per c c Of the latter 50 c c was the maximum for adults and the dosage was graded for children in the proportions of 1 c c per kilogram of body weight The serum was employed in the treatment of 1113 patients with diphtheria, and the mortality rate was 2.07 per cent. Excluding 5 patients who died within 24 hours after admission, the mortality rate was 1.62 per cent

Diphtheria toxin which circulates through the patient's blood before the administration of antitoxin may become fixed in certain tissues of the body and cannot be reached by subsequent antitoxin treatment K Kundratitz (Med. Klin 26:1289 (Aug. 29) 1930) tried a method recommended previously by Frohlich and Zak, of combining theophylline with diphtheria antitoxin to make the tissues more permeable In both animal experiments and clinical application, Kundratitz observed a lowered mortality with this treatment The method of administration was as follows:

Patients with severe infections were given 10,000 to 20,000 units of antitoxin intravenously followed in ½ hour by a subcutaneous injection of 0.5 to 1.0 c c of euphylline (a combination of theophylline and ethelenediamine) One-half hour later 10,000 to 20,000 units of antitoxin were given intramuscularly, followed in 6 hours by theophylline. This treatment was repeated in another half-hour, and 12 hours and 24 hours later. Patients given this drug must be observed for circulatory disturbances, and considerable fluid must be given to



prevent dehydration from the resulting diuresis.

**Human convalescent serum** has been used frequently in place of commercial antitoxins in the treatment of diphtheria. It is thought to contain other factors which are beneficial to the patient in addition to its antitoxin content. H. Hentschel (*Monatschr. f. Kinderh.* 48:50 (Sept.) 1930) employed such serum in the treatment of 7 patients, 2 of whom had mild, and 5 severe infections. The results were apparently better than those obtained in the average patient treated with commercial horse serum antitoxin. However, the membranes in these patients did not slough so rapidly as in the control series.

In the treatment of patients with *laryngeal diphtheria*, the mechanical removal of the membrane by means of **suction** has been employed in the hope of avoiding intubation or tracheotomy. Exceptionally good results have been described recently by D. M. Tolle (*loc. cit.*). Patients with laryngeal diphtheria were first given 20,000 units or more of **antitoxin** intravenously and then by direct laryngoscopy, the membrane was removed by **suction** through a metal catheter. This latter procedure frequently had to be repeated several times, once as often as 8 times. In certain patients, **intubation** was **necessary** also. The mortality of a series of 26 patients suffering from severe tracheobronchial diphtheria was 57.6 per cent as compared with 95.8 per cent in a similar group reported by another clinician who employed only the customary methods of intubation and tracheotomy. Comparing the whole group of 212 patients treated with suction by the author and a group of 697 reported from the same hospital 10

years previously and not treated by suction, the percentage of intubations was found to be reduced from 41 to 9.8. The mortality of the suction treated patients was 16.7 as compared with 41.6 per cent of the previous series. Certain types of diphtheritic laryngitis were not improved by suction such as (1) early infections in which edema was the outstanding feature and the membrane slight in amount and (2) very extensive membrane formations involving the bronchi and bronchioles.

With the knowledge that diphtheria toxin depletes the glycogen store of the liver and assuming that this organ cannot function properly in detoxifying the toxin of severe diphtheritic infections, L. Kostyál (*J. A. M. A.* 96:1329 (Apr. 18) 1931) Budapest correspondent, instituted **dextrose** and **insulin** treatment of 121 patients. Preliminary blood determinations were made and the dosage of sugar and insulin determined accordingly. Usually 10 to 20 units of insulin were given 2 to 3 times a day. Favorable results were observed, especially in the reduction of the mortality rate from about 27 or 32 per cent to 8 or 10 per cent. There was an improvement of the appetite and, even in fatal cases, the liver at necropsy was found to be well supplied with glycogen.

**Carriers.**—A new treatment of diphtheria carriers by means of **x-ray radiation** was instituted by R. Wahl (*Deutsche med. Wchnschr.* 57:276 (Feb. 13) 1931). He employed a Holfelder instrument with a lead glass tube 3.5 cm. in diameter. The central rays were directed to the tonsil from a submaxillary angle. The nose was also radiated. Thirty per cent of a skin dose was given to children of older age; less to infants. Of 133 persons harboring

diphtheria bacilli, and 3 with other pathogenic microorganisms in the nose and throat, 96 became negative after 1 treatment. Those remaining positive were again treated in 2 to 3 weeks' time with one-third of the original dose and the majority of these were then free from the infecting microorganism.

**IMMUNITY.**—The occurrence of clinical diphtheria in patients who have supposedly been immunized against that disease has raised some doubt in regard to the value of the *Schick reaction* as a test of immunity. B. Weill-Hallé, Gorostidi, Delthie and Papayannon (Bull Soc de pédiat de Paris 27:431 (Oct) 1929) observed 10 patients who had evidence of clinical diphtheria subsequent to their immunization. Three patients of this series had no membrane formation, however, and they were considered as carriers with a concomitant sore throat. In 3 other instances, the infection followed an attack of measles and the authors suggested that any severe illness may temporarily depress the diphtheria antibody content of a patient's blood.

Other studies, however, have indicated that the *Schick reaction* is not affected by intercurrent disease. B. Eddy and A. G. Mitchell (Am. J. Dis. Child. 40:985 (Nov) 1930) observed the *Schick reaction* of 358 individuals who were suffering from illnesses other than diphtheria, chiefly measles, scarlet fever, poliomyelitis, varicella and pertussis. These same patients were retested during and at the end of their convalescence. There was no appreciable variation in the percentage of positive and negative reactions obtained at these different stages of their illness.

In a study of this problem with determinations of the antitoxin content of blood serum, J. Siegel (München. med

Wchnschr 76:1632 (Sept 27) 1929) observed considerable variations in the same patient from time to time. Small injections of diphtheria toxin will produce a temporary lowering of antitoxin in the blood, causing the so-called "negative phase," which has been observed in patients immediately after the injection of immunizing material. One infant who had had a sufficiently large amount of antitoxin in his blood for protection, suddenly had a lowered content and during this period developed a clinical attack of nasal diphtheria.

Similar experiments have been made by R. G. Flood (Am. J. Dis. Child. 39:107 (Jan) 1930), who had been attracted to the study by the occurrence of diphtheria in persons who had had negative *Schick reactions* previously. He first developed a dilution of toxin and antitoxin which produced a skin reaction on a guinea-pig and yet no slough. It contained  $\frac{1}{450}$  of a minimal lethal dose of toxin. To this solution the blood serum of a patient was added and the absence of reaction or the production of a slough of the animal's skin indicated whether there was more or less antitoxin in the patient's blood than the supposed protective amount ( $\frac{1}{50}$  unit). Among a group of 15 children, 3 to 11 years of age, with negative *Schick reactions*, 46.6 per cent did not have  $\frac{1}{50}$  unit of antitoxin in their blood serum. However, it was observed that the injection of toxin-antitoxin caused a much quicker rise in serum antitoxin in those patients who had a relative high, though subminimal, antitoxin content. Young adults likewise responded quicker and to a greater extent to such injections than children.

The *Schick reaction* in relation to the morbidity of diphtheria varied somewhat in its accuracy, according to the

observations of E Merlino (Riv di clin pediat 28 789 (Sept) 1930, Am J Dis Child 41 180 (Jan) 1931) The reactions of mothers and of their infants were tested These were similar in 34 mothers and in their infants under 4 months of age, except in 1 instance, in which the infant had a negative Schick reaction and the mother a positive In 31 infants, 5 to 8 months of age, the reaction to the Schick test was different from that of the respective mothers in 16 instances When tests were made on a group of older children, 8 were found to be Schick-positive and yet were carriers of the diphtheria bacillus without having clinical evidence of the disease Two children with negative Schick reactions developed clinical diphtheria

It has been suggested that there are other factors of immunity to diphtheria than the antitoxin content of the blood F Hamburger and J Siegl (Munchen med Wchnschr 76 1537 (Sept 13) 1929) observed 20 patients with clinical diphtheria who recovered spontaneously without the aid of antitoxin Fourteen children and 1 adult had positive Schick reactions shortly after their attacks On retesting 8 of this group 4 to 23 months later, 6 had retained their positive Schick reactions Other observations which question the reliability of the accuracy of the Schick test are these (1) The occasional person with a negative Schick reaction who develops a clinical attack of diphtheria, (2) the many carriers of diphtheria bacilli with positive Schick reactions who do not contract clinical manifestations of the disease

This variation between the Schick test and the clinical disease of diphtheria has been approached from another viewpoint by M Mann and I J Kligler (J

Prev Med 3 309 (July) 1929) They performed Schick tests on some 3000 persons in Palestine and recorded percentages of positive reactions in age groups which corresponded very closely with those figures compiled by Zingher for the city of New York Clinical diphtheria, however, is far less frequent in the former locality The observers conclude that Palestine children have light attacks with few or no clinical symptoms, but have sufficient infection to produce an immunity

The so-called "negative phase" following diphtheria immunization is a temporary decrease of a patient's immunity occurring within the first 2 weeks after the first injection and disappearing from 1 to 3 weeks later All children do not have this negative phase but, according to J Siegl (Munchen med Wchnschr 77 1054 (June 20) 1930), the number is sufficiently large to be a warning against employing active immunization methods during severe epidemics or when a patient is a carrier with diphtheria bacilli in his nose or throat Investigation of the blood serum of 3 infants, 4, 6 and 8 months of age respectively, immunized with Ramon's toxoid showed temporary decreases of antitoxin content The antitoxin was lowered to one-half the original content the day after the injection In 1 instance on the second to fourth day, the titer of the antitoxin was lowered to one-fourth of its previous strength but returned to normal by the end of 8 days.

A few years ago Schick and Topper reported the rare occurrence of diphtheria in patients who had had their tonsils removed and that the percentage of negative Schick tests was much higher (82 per cent) in children who had had tonsillectomies than in average groups. Somewhat different results have been

obtained recently by K. D. Geddie (Am J. Dis Child 40 1032 (Nov) 1930), who performed Schick tests on 883 children aged 1 to 18 years. In 411 children who had not had their tonsils removed there were 13.6 per cent with negative Schick reactions. In 96 who had had tonsillectomies the percentage of negative was only 20.8. Administration of immunizing material to 2 such groups produced very little variation in the percentages made Schick-negative. The conclusions drawn from these figures tended to dispute the value of tonsillectomy in producing immunity in any significantly large number of children.

**Active Immunization.—Methods.—**

In regard to the relative value of *toxin-antitoxin* mixtures and *anatoxin* or *toxoid* for active immunization against diphtheria, several comparative studies of the last few years have favored the latter material. A. B. Schwartz and F. R. Janney (Am. J. Dis Child. 39:504 (Mar) 1930) compared the immunizing value of several types of toxin-antitoxin mixtures and toxoids. From 71 to 86 per cent. of a series of 477 susceptible children were made Schick-negative by toxin-antitoxin while 98 per cent. of a group of 128 children were made negative by formalin-treated toxin (toxoid). Mention was made of the point that serum sensitization was avoided by the use of the toxoid.

In a similar study by W. T. Harrison (Pub Health Rep. 45:1883 (Aug 15) 1930), a series of 475 children of school age were given toxoid injections and 95 per cent made Schick-negative while only 64 per cent of a group of 355 children were made negative by toxin-antitoxin injections.

In France, toxoid has been employed in the immunization of some 500,000

persons and in the experience of G. Ramon and G. I. Hélie (Am J Dis Child 39 685 (Apr) 1930) 96 to 100 per cent of this number were made Schick-negative 6 to 8 weeks after the last injection. In certain institutions the routine use of toxoid had almost eradicated diphtheria. The authors still employ 3 injections of 0.5, 1.0 and 1.5 c.c. with a 3-week interval between the first 2 injections and 2 weeks between the second and third injections.

In a subsequent report by G. Ramon and R. Debré (Am J. Dis Child 41 1 (Jan) 1931), 96 per cent of a series of 105 children were found to have  $\frac{1}{30}$  of a unit or more of antitoxin in their blood after treatment with toxoid, and all had negative Schick reactions. Children who remained Schick-positive after the routine treatment were given one or more additional injections until they became negative. Older children responded more quickly than younger ones to the immunizing treatment and had larger amounts of antitoxin in their blood. The older children were thought to have had a greater antitoxin content before treatment was begun, although the amount was insufficient to produce a negative Schick reaction. Observation of children for 2 to 4 years after their immunization indicated that the amount of antitoxin in the blood did not decrease in that time. In a series of 95 such patients, 95 per cent. still had enough antitoxin to make them immune 3 to 4 years later.

Within the last few years Loewenstein's method of immunization by cutaneous application of an ointment containing diphtheria toxoid and dead diphtheria bacilli has been more extensively used and produced favorable results. Although the percentage of patients made immune by this method is

never as high as that obtained by subcutaneous injections, there are distinct advantages of the ointment in that it is easy to apply and is not painful. In a report by E. Loewenstein (München med Wchnschr 77 883 (May 23) 1930) the children in 2 institutions in Vienna who have been treated with this method have been free from diphtheria in spite of a fairly virulent epidemic in the city. In the group of youngest children, 100 per cent had been made Schick-negative, among children 3 to 6 years of age, 87.5 per cent had been made negative, and in adults, 61 per cent were made negative. The ointment was rubbed into the skin 3 times, at intervals of 2 weeks. A month after the last inunction, immunity usually had developed. J. Siegl and K. Hassmann (München med Wchnschr 77 1665 (Sept 26) 1930) report favorably on Loewenstein's ointment but believe that the immunity develops slowly, in one group of 42 children, 4 months were required for the production of enough antitoxin to make positive Schick tests negative.

E. Nobel (Wien klin Wchnschr 44 75 (Jan 16) 1931) was able to obtain 35 per cent negative Schick reactions in a group of 206 susceptible children when tested 7 to 12 weeks after the last application. The same children were tested 3 months later and the same percentage of the group was negative. Although he acknowledges certain advantages of the ointment, such as the ease of application and painlessness, he stresses the fact that the method is not as efficacious as others have been.

The use of Loewenstein's ointment for immunization purposes has been employed in the United States by A. F. Abt and B. F. Feingold (Am J. Dis. Child 41 8 (Jan) 1931). A series of

62 children, 11 months to 17 years of age, were given 3 rubs with this ointment and 2 to 7 months after the last application Schick tests were repeated. Of the group, 70.9 per cent had become Schick-negative. This figure compared favorably with those obtained by European investigators. There has been some indication that immunity from this type of treatment develops slowly and if the Schick tests are performed at longer intervals after the last cutaneous application, they are more apt to be negative.

A similar study in this country has been made by A. H. Kegel and B. M. Gasul (Am J Dis Child 41 45 (Jan) 1931). A number of children were Schick tested and on 47 who reacted positively the ointment was applied 3 times at intervals of 10 days. The ages ranged from 1 to 10 years. Six weeks after the last application of ointment the group were again Schick tested and 55.3 per cent had been made negative.

Certain modifications of Loewenstein's method of immunization have been made by H. Baar and H. Benedict (Ztschr f Kinderh. 50 195, 1930). Mustard oil was first used as the vehicle for the material in order to produce an irritation of the skin and stimulate absorption of the material. Subsequently, mustard plasters were found more suitable in that they did not produce such an odor. In a review of the results from the immunization of children by the percutaneous method, the authors reported that a small number who had been made Schick-negative became Schick-positive after 2 years. A single application of the ointment again made them negative.

There has been corroboration of the work of Loewenstein in regard to the production of an active immunity by

cutaneous application of **diphtheria toxoid** in an ointment. A Besredka (Ann Inst Pasteur 46 542 (May) 1931) employed a similar method in rabbits, first producing a hyperemia of the skin and then rubbing in an ointment consisting of 2 parts of **lanolin** and 1 part of **vaseline** to which was added  $\frac{1}{25}$  to  $\frac{1}{100}$  c c of **toxin**. Several treatments were given and the animals developed an active immunity and subsequently resisted the injection of large doses of diphtheria toxin

Other methods of preparing material for active immunization against diphtheria have been developed in the last few years with the hope of finding a substance which is effective but produces less reaction when injected. Of considerable interest are the **diphtheria toxin-antitoxin floccules**. When toxin and antitoxin are mixed together, a precipitate forms in the form of floccules. This precipitate, washed and dissolved in saline solution, has antigenic properties. Subsequent investigations have shown that **toxoid** mixed with **toxin** also produces a precipitate and produces a material devoid of any danger from the presence of free toxin. Both types of floccules have been used for immunization against diphtheria and have the advantage of a low nitrogen content and consequently produce very little reaction in the patient. R. Swyer (Lancet 1·632 (Mar 21) 1931) employed **diphtheria toxoid-antitoxin floccules** in the immunization of 87 nurses with positive Schick reactions. Usually 3 injections of 1 c c were given at 2 weeks' intervals. Of the entire group 68 were retested 6 to 8 weeks after the last injection and 64 were found to be negative. The author was gratified to note that the reactions to injection were not severe; in only 5 instances was

there any general reaction, 3 of whom had slight malaise and vomiting.

**Killed diphtheria bacilli** have been added in many immunization mixtures to produce bacterial antibodies against diphtheria in addition to **antitoxin**. E. J. Gen and L. T. Tchertkov (Vrach Gaz 6 422 (Mar 31) 1931, J. A. M. A 97 585 (Aug 22) 1931) attempted to immunize guinea-pigs against diphtheria with killed diphtheria bacilli but were unable to do so and subsequent infections with diphtheria bacilli caused death of the animals. It was concluded that this method has no value in producing immunity and the production of antitoxin in the blood is the essential factor in the development of immunity against the disease.

**Combined Immunization.**—Combined immunization against *diphtheria* and *scarlet fever* has been attempted recently. The 2 microorganisms were grown simultaneously on suitable media and the toxin filtrate treated with formalin. O. Nureddin (Compt rend Soc de biol 103 1200 (May 1) 1930) has tried this method. The resulting toxoid was standardized in regard to its diphtheria toxin content but the amount of scarlet fever toxin could not be determined. A small group of children, 6 to 15 years of age, with positive Schick and Dick reactions were given 3 injections. Six weeks after the last injection 81 per cent had negative skin reactions to both the Schick and Dick toxins.

More recently other investigators have directed efforts towards standardizing the toxin from each microorganism grown on separate media, treating each with formalin, and finally combining the 2 toxoids into one solution for injection.

C. Dopfer (Bull Acad. de méd. Paris 105 794 (May 19) 1931) employed combinations of *typhoid vaccine*



and diphtheria toxoid in the immunization of certain French Army recruits who were Schick-positive. There were no deleterious effects, immunity to both diseases being produced. Ramon and Zoeller, and others had previously shown that in combined vaccination of this type, there is probably a reinforcement of the antigenic properties of each. In Dopter's series the incidence of diphtheria has been reduced and that of typhoid remained as formerly at zero.

**DISLOCATION.**—In a study of 30 cases of *dislocation of the cervical vertebræ*, Mitchell Langworthy (J A M A 94 86 (Jan 11) 1930) observed that dislocation occurs more often in the upper cervical spine. The cause may be from minor injury such as coughing or sneezing. Seventeen of the cases were bilateral. Langworthy got excellent results by using the **manipulation** described by Walton. It consists essentially of bending the head away from the side of the dislocation, rotating the head toward the side of the dislocation, and then hyperextending the cervical spine. A **plaster** is then applied to maintain the correction. The identical procedure is carried out in case of double dislocation—one side is reduced at a time. The dislocation consists of a set of cervical vertebræ sliding upward on the facet of the vertebræ next below and catches on the top of the lower facet, or slips over to the intervertebral notch in front of the lower facet.

*Habitual dislocation of the shoulder* is rare. M. S. Henderson (J A M A 95 1653 (Nov 29) 1930) describes 37 cases in which 40 operations had been performed from 1912 to 1930. In the 37 cases, the one definite etiological factor was primary traumatic dislocation. Laxness of the anteroinferior portion of

the capsule is the cause of habitual dislocations in many of the cases. The history is that following trauma and subsequent reduction of the dislocation, the arm had not been protected adequately or for a sufficient period of time. Pain is severe and unrelieved until reduction is accomplished. Subsequent dislocations may occur without trauma or violence. Habitual dislocations are almost always of the subcoracoid type, with the head of the humerus resting beneath the coracoid process. Posterior dislocations are usually not so painful and may be of the snapping variety. Twenty-five of the 37 patients observed by Henderson were males and the age limit was 20 to 40 years.

Conservative treatment is limited to the use of an apparatus that acts as a check to abduction and forward elevation of the arm. Some shoulders may be corrected by such apparatus treatment. Frequently, however, the dislocations become increasingly common and **surgical intervention** is necessary. Five types of operations for prevention of dislocation of the shoulder are described: (1) Those performed on the bony structure, (2) those on the capsule, (3) muscle transference and muscle lengthening, (4) check and block operations on the bone or ligaments, and (5) suspension operations.

**Anterior capsulorrhaphy** was done on 16 of the cases with cure in 37.5 per cent. Three cases were operated by **posterior capsulorrhaphy** for posterior dislocation and these remained well. Of 8 operated with the **Clairmont method**, more than 5 years ago, 50 per cent of the patients remained well. **Tenosuspension** on 10 patients cured all.

For *congenital dislocation of the hip* **manipulative reduction** should be em-

ployed at the earliest stage, in the opinion of E L Evans (Brit M J 2 1035 (Dec 20) 1930) In children under  $2\frac{1}{2}$  years, the reduction may be brought about with ease while the adductors are being gently stretched In older patients, however, if an early reduction is not obtained, 2 further attempts at intervals of 7 to 10 days are advocated, when reduction without force will usually be accomplished Following 3 unsuccessful attempts, **capsulotomy** is indicated If redislocation occurs after successful reduction, and the dislocation is due to failure of growth of the superior and posterior borders of the acetabulum, the border should be levered over the head and held by a **bone graft** The age limit for manipulative reduction is 7 to 8 in unilateral, and 5 to 6 in bilateral cases Beyond these, **open reduction** is indicated

The abnormal movements permitted by methodical suppression of different ligaments were studied by P Guedj (Rev d'orthop 38 29, 1931), who at the same time noted the ligamentous lesions causing the abnormal movements and the exaggerated physiological action A lesion of the crucial ligaments is essential for all luxations of the *knee* forward, backward, outward and inward, but is not always sufficient alone to permit a luxation Forward luxations are the most frequent, and usually hyperextension is a causative factor Rupture of the skin, rupture or compression of the popliteal arteries, and laceration and stretching of the external popliteal sciatic nerve are frequent complications

Posterior and outward luxations are the most frequent of posterolateral luxations Laceration of both crucial ligaments is always accomplished by laceration of at least one lateral

ligament **Immediate reduction** should be performed and followed first by immobilization for from 10 to 15 days and then by **massage** and easy **passive motion** *Recurring luxation* should be treated by **continuous extension** and **prolonged immobilization** Prognosis of traumatic luxation depends to a great extent on the condition of the lateral and posterial ligaments Vasculoneural complications and irreducible luxations require immediate operation When the meniscus is involved it should be removed, and articular foreign bodies should be removed if they are free or attached to the extremity of the crucial ligament Vasomotor disturbances can be benefited more by operation of the sympathetic nerves than by massage, counterirritants or hydrotherapy

**DIVERTICULUM OF COLON.**  
See COLON

**DUODENUM.—CARCINOMA.**  
—*Surgical Treatment.*—J Meyer and D H Rosenberg (Arch Int Med 47: 917 (June) 1931) report 4 cases of primary carcinoma of the duodenum The authors recommend early surgical intervention, the type of operation depending on the presence or absence of jaundice or metastasis In instances without the aforementioned complications, wide **excision** is advocated With the development of metastasis, or if the general condition is too poor to permit resection, a palliative **posterior gastroenterostomy** should be performed When duodenal carcinomas are associated with jaundice, such as in the periampullary form, they are best treated by preliminary **cholecystogastrostomy**, **duodenostomy**, or **enterostomy**, followed later by either **posterior gastroenterostomy** or **resec-**

tion, depending on the exigencies of the cases

**CHRONIC STENOSIS.**—*Etiology.*—In discussing chronic duodenal stenosis, R. Appelmans, F. Van Goodsenhoven and J. Boine (Rev belge sc méd 1.1 (Jan) 1930) state that the causes of this condition may be compression where the superior mesenteric artery crosses the ascending third portion of the duodenum; a short mesocolon with resulting compression of the duodenum by the middle colic artery, congenital bands (primary periduodenal adhesions), secondary adhesions from ulcer or cholecystitis, pressure from a tumor in the neighborhood

*Symptoms.*—The symptoms of this condition are daily aching epigastric distress occurring periodically after eating, with nausea, at times vomiting, sometimes simulating gastric crises. Lying prone generally gives relief.

*Diagnosis.*—From the x-ray examination the diagnosis is certain from demonstration of dilatation of the duodenum, stasis of its contents, and exaggerated peristalsis and antiperistalsis, with more or less spectacular return of the duodenal contents into the stomach. The pylorus remains patent at all times. Examination in the erect position is more fruitful than examination with the patient horizontal. Examination of the colon by opaque enema helps to differentiate between the above listed causes. When the stenosis is due to pressure from the middle colic artery it may be possible to demonstrate that the obstruction is relieved when the colon is empty and is exaggerated when the colon is filled.

*Treatment.*—Surgical treatment by duodenojejunosomy or gastrojejunosomy gives excellent results. Medical treatment may be efficacious and con-

sists in appropriate abdominal support, strengthening exercises for the abdominal muscles and appropriate treatment of constipation when it exists. The use of the prone position or knee-chest position after eating is of value

**DYSPEPSIA, CARBOHYDRATE.**—A. F. Hurst and F. A. Knott (Quart J Med 24:171 (Jan) 1931) state that intestinal carbohydrate dyspepsia is one of the commonest abdominal disorders. Starch digestion is accomplished by the ptyalin of the saliva, the amyllopsin of the pancreatic juice, and the diastase of the juice secreted by the small and large intestines, according to these authors. They have shown that salivary digestion is relatively unimportant, and that amyllopsin is not the most important diastatic ferment, since starch digestion is often normal in severe pancreatic disease. Diastatic ferments have been obtained from the duodenum in obstructive jaundice when trypsin was absent and the gastric secretion was normal, proving, to their opinion, the presence of an active diastatic ferment in intestinal juice.

In refuting the former belief that starch in vegetable cells could be digested only when the cellulose envelopes had been broken by cooking, or by bacterial action, these writers point to investigations proving that cellulose walls of vegetable cells are not broken by cooking, and that the acidity of the intestinal tract from the duodenum to terminal ileum prevents the growth of fecal types of organisms believed to cause the digestion of cellulose. "It is clear," they state, "that in normal people the digestion of starch and the absorption of the products of its diges-

tion occur in the almost complete absence of bacteria." Hurst and Knott have seen that when carbohydrate food, prepared in the ordinary way, is eaten, some of it reaches the small intestine as starch completely freed from its envelopes and some as large swollen, but unruptured grains. They have shown that ferments can enter these swollen grains and digest and extract the starch within them. Such activity is not possible in uncooked starch grains. Plates of these findings are included in the paper.

**ETIOLOGY.**—Intestinal carbohydrate dyspepsia results when the secretion of the small intestine is deficient, allowing some undigested starch to reach the cecum, according to these authorities. Here, diastase of the cecal secretion penetrates the cells giving dextrins and sugars upon which saccharolytic bacteria flourish, with resulting gas formation. Symptoms are due to the presence of carbon dioxide, and acetic, butyric and other organic acids. The writers believe that this condition can only arise when the small intestine is damaged in the presence of normal stomach and colonic activity. In cases of achlorhydria, starch digestion is accomplished by salivary ptyalin, while in colitis hypermotility is the rule and excessive fermentation cannot occur.

#### **SYMPTOMS AND DIAGNOSIS.**

—Symptoms of this disorder include a widespread feeling of discomfort and fulness in the lower abdomen due to gaseous distention of the colon. It is most noted just after meals (gastrocolic reflex) and before defecation. The discomfort is often most severe at night. Acute pain due to colonic spasm is not infrequent, according to the authors. Excessive amounts of odorless flatus is often expelled with some relief. Con-

stipation may result from induced spasm, but a mild diarrhea is more common. Normal bowel movements are frequently present. Fecal examination reveals large numbers of starch granules, which are stained blue-black with iodine. Few or none are present normally. The stool differs from that in pancreatic insufficiency in that there is no excess of fat or striated muscle. Bacteriologically, there is a great increase in the enterococci due to the favorable medium. Their presence is undoubtedly a result and not the cause of the condition, according to the writers. The stools are acid or become so very quickly, and bacteriologic examination reveals an increase in the aciduric bacilli (*B. acidophilus*, *B. bifidus*, etc.) and the coarser micrococci. Ordinary plate cultures of the feces have been sterile because of the acidity and the predominance of the aciduric strains. A simple fermentation test devised by Schmidt and Strasburger is diagnostic of this condition. A small quantity of feces is mixed with water and incubated for 24 hours, any gas given off being collected. No gas is evolved from normal stools, while in carbohydrate dyspepsia large amounts of odorless gas may be produced. In putrefactive conditions foul gas is produced and the feces become strongly alkaline.

**TREATMENT.**—*Diet.*—The treatment, according to Hurst and Knott (*loc cit.*), is very simple. "Sugars are perfectly digested, and in all but the most severe cases in which chronic diarrhea is present, free starch, as in flour and bread, is well digested, as the pancreatic amylase can very easily deal with this. As there is very little starch in green vegetables, it is also unnecessary to prohibit them, unless irritation of the intestines by the products of fer-

mentation has been sufficiently great to make it necessary to avoid anything which irritates the mucous membrane mechanically. In severe cases, therefore, it is best to exclude vegetables of every kind and also rice. In milder cases, and in more severe ones as soon as the diarrhea has ceased, green vegetables can be allowed as purées, and at a still later stage there need be no limitation of anything but root vegetables, cauliflower and rice. In most cases, after a comparatively short time it is possible to make the restrictions gradually less severe until finally nothing but

potatoes are prohibited." The changes in the diet are indicated by stool examination, which should not reveal an excess of starch, or gas on fermentation.

The authors have used an active preparation of **amylolytic ferment** with each meal, preferably a vegetable diastase rather than pancreatic ferments. **Powdered charcoal** may be of assistance in some cases. In *diarrhea*, **powdered chalk** is suggested. Inasmuch as the excessive growth of enterococci is purely secondary, the writers condemn the use of vaccines as being futile, as are also colonic irrigations.

## E

**ECZEMA.\*—ETIOLOGY.**—In a patient hypersensitive to some irritating agent, eczema is apparent first as an erythema, then as edema with vesiculation. S. W. Becker (J A M A 97 983 (Oct 3) 1931) points out that no clinical or histological variations exist between eczema with its hypersensitivity and dermatitis venenata or simple dermatitis. The author cites Pusey, who states that when a balance exists between the capacity for resistance of the skin and the insults to which it is exposed, the skin is healthy, this balance may, however, be overthrown by variations of either factor, *i e*, by exposure, on the one hand, to insults beyond the capacity of the skin to resist, as dermatitis venenata; or, on the other hand, by a lowered resistance of the skin, so that it reacts from insults that the normal skin bears without apparent damage, which is eczema.

The usual types of irritants that cause most of the cases of eczema are

as follows: physical, represented by solar eczema; chemical, which is by far the most numerous. The author also describes his own series of cases as frequently due to primrose, poison sumac, the photogravure section of a newspaper, and the preparations for scalp treatments. Irritating products from organisms, as pyogenic bacteria and fungi, are classed as chemical irritants and are responsible for the so-called infectious eczematoid dermatitis found in areas bathed by purulent discharges. Dermatomyces is caused by a fungus which propagates in the stratum corneum, giving off a toxin which acts on the living epidermal cells. The reaction may be negligible, depending on the sensitivity of the patient, with but slight maceration, or it may be markedly erythematovesicular and constitute a true eczema.

**DIAGNOSIS.**—Becker (*loc cit.*) states that whereas the diagnosis of eczema would seem to be simple, many stumbling blocks exist. There is a lack of critical analysis of the dermatosis

\* See also article on Allergy

itself and the fact that many patients have already used irritating applications, thereby causing, as a rule, dermatitis venenata, complicates the picture. Eczema is a diffuse eruption involving moderately broad areas, frequently the exposed surfaces as the hands, arms, face and neck. Various parts of the body differ in sensitivity, as proven by numerous case histories. Furthermore, a localized type of eczema, characterized by sudden outbreak involving the flexures of the elbows, axillary folds and the inner extremities of the shoulders, has been described.

**TREATMENT.**—This depends upon the ability to ascertain and remove the cause. An expert history often reveals one or more possible etiological agents and verification can be made by means of the *patch test*, which consists of the simple application of suspected substances. A small amount of the materials suspected is applied to normal skin and allowed to remain from 24 to 48 hours, unless itching or burning is experienced earlier. A positive reaction is revealed by erythema followed by edema and vesiculation.

Desensitization therapy, in Becker's opinion, is a disappointment. The chief measures for alleviating suffering from eczema are local. The external treatment is largely protective, because the inflamed skin has lost its normal protective factors. Too frequently patients have perpetuated their eczema by irritating agents from either their own or their neighbors' stock of remedies.

During the vesicular stage, wet dressings of **potassium permanganate**, 1 grain (0.065 Gm) to a pint (500 c.c.) of water, prepared fresh twice daily, is effective. The dressings should be kept wet but not dripping. After the more acute signs have subsided, a **sulphon-**

**ated bitumen zinc paste** is recommended. Sulphonated bitumen N F, 1.8 Gm (28 grains), zinc oxide, 15 Gm ( $\frac{1}{2}$  ounce), sufficient petrolatum to make 60 Gm (2 ounces). This is recommended applied with a smooth wooden tongue blade, and as thick as butter. It should be renewed morning and night, after gentle removal with olive oil. Water, and more particularly soap, should be avoided.

*Lichenified eczema*, more uncommon than that previously described, should be treated by stronger applications, only after the sensitivity of the skin has been tested by a mild preparation of **sulphonated bitumen zinc paste**. If no inflammatory reaction occurs, the sulphonated bitumen may be replaced by **salicylic acid** and **pine tar**, beginning with 0.5 per cent. of each and increasing the strength cautiously.

**ECZEMA, INFANTILE.—ETIOLOGY.**—A study of 118 infants with various eczema-like cutaneous eruptions was made by H. Montlaurs (Nourrison 19.161 (May) 1931) with a view to ascertaining the possibility of the *enterococcus* as an etiological factor. A certain proportion of cutaneous reactions considered as infantile eczema show a common bacterial etiology of digestive origin and are found in infants between the ages of 1 to 5 months. These dermatoses, of which the so-called seborrheic eczemas are frequent, always begin on the buttocks, and the initial lesion represents a type known as infantile dermatitis. At this stage, it is a bacterial dermoepidermitis and bacteriological research reveals constantly the presence of *enterococcus* in the epidermal scales. Coprologic examination shows pullulation of the *enterococcus* and exaggeration of the normal fermen-



tative process, with an increase in the amount of organic acids. This exaggeration is present only in the breast-fed infants. The digestive disorders that accompany the so-called eczema are probably due to a hepatopancreatic deficiency, in which syphilis may play a rôle. **Antienterococcal vaccination** by intradermal injections frequently brings rapid cure of the dermatosis, as well as an amelioration of the digestive condition.

*Facial eczema* in male infants is due, according to G. W. Bamber (Brit J Dermat 43 279 (June) 1931), to an erythemato-urticarial reaction or a primary pruritus and is 3 times as common in males as in females. Fat babies are most frequently involved. Exacerbations are associated with gastrointestinal disorders and with asthma. A family history of some allergic phenomena is not rare. There appears to be some constitutional peculiarity adherent in the infant. External factors, cold weather and other variations in temperature, are extremely important, and infection of the skin is neither constant nor necessary.

**TREATMENT.**—In an article by Lewis Webb Hill (J A M A 96 1277 (Apr 18) 1931) upon this subject, the importance of a milk-free diet for eczematous infants sensitive to casein and lactalbumin is set forth and a preparation is described which meets this requirement. It consists of.

	Per Cent
Soy bean flour	67.5
Barley flour	9.5
Olive oil	19.0
Sodium chloride	1.3
Calcium carbonate	2.7

This is a light brown flour of which 6 level tablespoonfuls added to 7 ounces (210 cc) of water constitutes "full strength" and contains.

	Per Cent
Fat	28
Carbohydrate	40
Protein	40
Salts	10

One fluidounce (30 cc) contains 17 calories. Unless stools are loose, a level tablespoonful of a mixture of maltose and dextrose is added, bringing the carbohydrate percentage to about 7.

Infants less than 8 months old should be started on two-thirds strength, or even weaker for younger babies for the first few feedings.

The health and nutrition of babies is well sustained by this mixture and decided benefit to the skin eruption is observed in a good proportion of cases.

Prolonged boiling of milk causes some change in the proteins which render them less likely to cause symptoms in a sensitized baby.

**Evaporated milk**, which is heated to 240° C in the process of manufacture is recommended as a substitute for ordinary milk in mild cases in which it is not desired to substitute the "Sobee."

Irene Waters (J Allergy 2.225 (May) 1931) based on experience in the Department of Nutrition, Presbyterian Hospital and the Department of Dermatology, Vanderbilt Clinic, New York City, states regarding the use of sobee: "In our experience, even after prolonged use, the growth record of children fed on sobee compares favorably with the growth of children fed on cows' milk. The only contraindication to its use has been in infants sensitive to barley, one of the ingredients of sobee."

**EMPYEMA. — ACUTE. — Treatment.**—Emphasis is laid on the necessity of recognition of the relation of acute empyema to the pneumonic process, whether synpneumonic or metapneumonic, by C. A. Hedblom (J A.

M A 97 1943 (Dec 26) 1931) as determining the course of treatment In the synpneumonic group, where streptococcus is most often found, **aspiration** alone, to the point of securing cardiac and respiratory relief, should be repeated as often as necessary He says, "It is the most conservative and proper method of relieving mechanical embarrassment during the synpneumonic stage preparatory to instituting closed drainage, and it is particularly valuable in infants" A cure may be effected in a small empyema due to mild infection Such simple procedure in this very early period fulfills Hedblom's requirements that "the fundamentals of treatment would seem to be drainage without embarrassment of respiration and circulation, reexpansion of the lung, and general supportive measures."

When the process is evidently metapneumonic, or when, after repeated aspiration it is recognized that aspiration alone will not effect a cure, though it has played a vital part in carrying the patient through the period requisite for encapsulation and mediastinal stiffening, consideration of the method of freer drainage becomes necessary. The arrival of this stage of the process is recognized by change in the character of the exudate from the serohemorrhagic or seropurulent of the early period, to a frank purulent material The question regarding drainage centers primarily about whether it shall be open or closed and secondarily deals with variations in either method

Hedblom (*loc cit*) states that **closed drainage** can be made to approximate simple aspiration as an operative procedure. It can easily be done in the patient's room The technic which he has followed with much satisfaction for 12 years is essentially as follows Un-

der local anesthesia a catheter (22 F) is inserted through an ordinary bladder trocar and cannula, which it just fits, and fastened in place after the method described by Mazingo and recently by Alexander **Pus** is then **aspirated** by means of a 60 to 120 c c glass syringe If the patient is an adult and the cavity is large, from 200 to 300 c c is drawn off The tube is then clamped and the piston of the syringe is removed **Saline solution**, in amount a little less than the amount of pus evacuated, is then introduced by gravity through the barrel of the syringe used as a funnel The same amount of the mixture of pus and saline solution is now aspirated, a syringe-ful being first reinjected a few times to bring about a complete mixture The process is repeated until the solution returns fairly clear The process is repeated every 2 hours during the day and once or twice at night while the patient is toxic and the cavity large If there is no evidence of bronchial fistula, *e g*, no cough and sputum and no irritation during the irrigation with saline solution, surgical solution of **chlorinated soda** is substituted after the first 2 or 3 irrigations In infants a smaller catheter is used and only small amounts of pus are withdrawn before saline solution is substituted. In this way there is no appreciable fluctuation in intrathoracic pressure By this simple method the cavity is not only kept emptied of pus, but its walls are washed mechanically clean, fibrin and necrotic material are dissolved, and, if surgical solution of chlorinated soda or other bactericidal solutions are used, the surfaces are at least partly sterilized The lung is kept partly expanded from the onset of treatment

J A Danna (J. A. M. A. 96:1452 (May 2) 1931) reports the treatment of

empyema by aspiration and air replacement without drainage in a series of 35 cases, with loss of but 2 patients, approximately 7 per cent. He found that by replacing these contents gradually with an equal volume of air, the existing relations of all structures are not interfered with, so that no trauma of any kind is done. The technic is described as follows:

A point that is located in the intercostal space corresponding to the lowest point of the empyema cavity is anesthetized with  $\frac{1}{2}$  per cent novocaine, infiltrating all the tissues from skin to pleura inclusive. A large needle is now attached, *by a stiff rubber tube connection* to a 50 or 100 c c Luer syringe and inserted at this point. A syringe of pus is now aspirated, the tube is clamped with hemostatic forceps, the syringe is disconnected, emptied, filled with an equal quantity of air and reconnected to the tube and needle, the forceps are unclamped, and the contained air is injected. This alternate aspiration of fluid and injection of air is repeated until, on aspiration, air comes through the needle, which shows the needle point is now above the fluid line or all the fluid has been aspirated. The patient and the needle are manipulated so as to make sure the needle rests in the bottom of the pus cavity, and the procedure is repeated until air again comes from the needle, which indicates that no more fluid remains. This is preferably done with the patient sitting up, but very sick patients are treated lying down with the head and shoulders slightly elevated.

When the amount of pus is large, a second spot in the chest wall is infiltrated with the anesthetic solution and a second smaller needle is introduced. The first large needle is connected to the suction apparatus and the second needle

to some form of pneumothorax apparatus whereby the amount of air that comes through can be measured. The suction apparatus is now turned on, and the pus is rapidly withdrawn. As each 100 or 200 c c of fluid is drawn into the suction chamber, a corresponding quantity of air is injected, thus, the architecture of the cavity, as it were, is not altered, and the hydrostatic or rather the physical compression of the lung is undisturbed, the inelastic fluid mass being replaced by an elastic air cushion.

The amount of pus removed varies from a few cubic centimeters to as much as 3000 c c at one time. The procedure is repeated as often as the fluid accumulates, on an average of about every 6 days.

That this simple procedure alone cannot be depended upon is admitted by the author. In some cases the fibrinous exudate prevents complete emptying of the cavity by blocking even the largest needle, rendering it possible to aspirate at most, only from one-half to two-thirds of the contained pus. Two courses have been followed in meeting this situation:

1. With the exercise of patience, the fibrinous exudate will eventually liquefy. The writer has been on the point of making an incision in a number of these patients, but after repeated aspirations the contents finally became completely fluid, and it was possible to empty the cavity entirely. The writer suggests that if surgical solution of chlorinated soda were used, it might, as happens in the drainage cases, cause a solution of the exudate and shorten the period of treatment. He has, however, purposely not done this in order to prove definitely that an empyema cavity will heal without any further aid than the removal of its contents.

2 In 5 cases in which the largest available needles became blocked, a small intercostal incision was made, just large enough to introduce the index finger; the patient was turned so that this incision lay at the most dependent part of the cavity, and he was instructed to perform repeated forced inspiration and expiration while forceps kept the incision open, masses of fibrin being removed by the same forceps as they appeared in the wound, until the entire cavity was thoroughly emptied of fluid and fibrin. If the patient becomes shocked or has a tendency to cough, the wound is closed by digital pressure, and the patient is immediately relieved. After a moment, the procedure is continued as before. When the chest has been entirely emptied, the patient takes a final deep inspiration, at the end of which the lips of the wound are compressed digitally and kept so by a gauze compress. These wounds do not drain; they heal readily and have to be reopened if the procedure is to be repeated.

[We believe that in the early synpneumonic conditions this procedure has a valuable protective element, for it has been the experience of the editor to find in a child, in whom cardiac and respiratory embarrassment again appeared on the day following an apparently most successful simple aspiration, that the reappearance of the embarrassment was not the result of rapid reaccumulation of fluid, as has so often been seen, but due to the rupture, and subsequent collapse, of the lung with complete pneumothorax. The author quoted truly appraises the situation, I believe, in the remarks which follow—EDITOR.]

If an attempt is made to empty the chest of the fluid accumulation by simple aspiration, and without air replacement, eventually it will have to be stopped without removing all the fluid for one of two reasons: either the negative pressure becomes so great as to cause pain

or respiratory or cardiac embarrassment, or the needle will come in contact with the visceral pleura and cause pain, coughing, dyspnea and shock.

If instead, the fluid is gradually replaced with air as it is removed, the cavity maintains its original size and shape, and every drop of the fluid can be removed with practically no discomfort to the patient.

[The inclusion of the thoracotomy, even if small, makes this a combination and not a simple aspiration procedure. In metapneumonic or other cases in many instances it must be followed with a painstaking and persistent enthusiasm, for the writer speaks of some of the cases refilling in spite of repeated aspirations "for periods as much as 5 and 6 weeks." His caution "This method calls for constant attention and the expenditure of much time, patience and thought by the surgeon himself, and is not to be lightly undertaken by a medical man or one not prepared for every possible surgical contingency," is well given—EDITOR.]

Because of the difficulty in securing solution of large firm coagula, and believing in the advantages of a closed method of treatment in aiding lung expansion, E. Heller (Arch. f. clin. chir. 157.281, 1929) favors a primary wide thoracotomy for removal of fibrin coagula, resuture of the wound and then the closed method.

Other solutions besides surgical solution of chlorinated soda are recommended. Optochin (ethylhydrocupreine) in solution has again been recommended as an irrigating and replacement fluid. P. Woring (Rev. franç. de pédiat. 5:60 (Feb.) 1929) reports on 36 cases where he employed an irrigation with  $\frac{1}{2}$  per cent solution and then instillation of 5 per cent solution in sufficient amount to provide a total of 25 mg. ( $\frac{3}{8}$  grain) per kilogram ( $2\frac{1}{8}$  pounds), though never a total amount over 0.5 Gm ( $7\frac{1}{2}$  grains). **Aspira-**

tion, with irrigation and replacement was sufficient in 24 cases. Six died, a mortality of 16.7 per cent, and 5 required more extensive treatment. They report no deaths in the group of children in the second year. [These results appear no better than those of McEnery and Brenneman on aspiration alone—Ed.]

Because of the same type of specific lytic effect on pneumococci, bile salts, sodium taurocholate in 5 per cent solution, is again reported on favorably by Castellanos (J de méd d Paris 29 48, 1931), employed after the method of Cocchi in 1927.

**CHRONIC.—Treatment.**—The reaching of the chronic stage by an empyema may be caused by delayed, ill-judged, or inadequate surgery or by the nature of the pathologic process itself. Hedblom (*loc cit*) considers that chronicity is usually due to inadequate treatment but may develop in spite of the best possible treatment. In 50 per cent of 310 cases under his observation, chronicity was judged to have been due to inadequate drainage, in the sense that it was not maintained until the cavity had become obliterated. It may be due to late primary drainage, to too early open drainage, resulting in extensive or complete pneumothorax, collapse of the lung, to bronchial fistula, to foreign bodies and to fibrosis of the lung.

That obliteration of the cavity may be secured with a minimum of life risk and deformity, expansion of the lung to the fullest possible extent should be sought for before mutilating surgery is done. Hedblom (*loc cit*) states that in his experience, it has been possible to secure a partial reexpansion of the lung, varying from 50 to 90 per cent, in more than two-thirds of the cases without bronchial fistulas, by irrigation

with surgical solution of chlorinated soda. There is always a marked improvement in the patient's general condition as evidenced by gain in weight and strength, often to a marked degree. The infection is greatly reduced in amount and virulence, even if the cavity is not entirely sterilized. The magnitude of the operation is thus reduced, the patient's condition for operation improved, and the operative field prepared.

The extent of operation necessary for obliteration of the cavity depends on its size and situation, varying from the simple Estlander to the most comprehensive, graded operation where there has been total permanent collapse. In case of total permanent collapse of the lung of long duration, a decortication usually fails. Extra pleural posterior thoracoplasty followed by outer or lateral costectomy with final removal of the roof of the residual pocket, according to the experience of Hedblom (*loc cit*), will bring about the complete healing of any cavity regardless of its size, including cavities with complete collapse of the lung.

**TUBERCULOUS.—Treatment.**—A sterile tuberculous empyema without clinical evidence of pulmonary tuberculosis, according to Hedblom (*loc cit*), is treated on diametrically opposite principles to those governing treatment of a sterile tuberculous empyema with active pulmonary tuberculosis on the same side. In the first instance an effort is made to obliterate the cavity by securing reexpansion of the lung. In the latter, treatment is directed to keeping the tuberculous lung collapsed.

The treatment of a sterile tuberculous empyema of the idiopathic type is aspiration of the pus, filtered air being substituted in such amount that the intrapleural pressure is above atmospheric.

The procedure is repeated at intervals as the pus accumulates. Absorption of the air into the blood stream creates a less than atmospheric intrapleural tension, which tends to reexpand the lung. If pus continues to reaccumulate after from 6 months to a year of such treatment, and the lung shows no evidence of extensive reexpansion, a graded **posterior extrapleural thoracoplasty** is indicated.

*Sterile tuberculous empyema with associated active tuberculosis* is treated similarly, except an attempt is made to prevent expansion of the diseased lung by keeping the pneumothorax pressure atmospheric or positive. If pus reaccumulates indefinitely, it constitutes the same indication for thoracoplasty as in the case of the idiopathic type.

E. A. Graham (Missouri M. A. J. 26:583 (Dec.) 1929) reports a group of 5 tuberculous empyema cases in which **extrapleural thoracoplasty** restored 4 to clinical health and he feels that the series of 80 per cent recoveries illustrates the value of the procedures where nonsurgical treatment means 100 per cent mortality.

**ENCEPHALOMYELITIS.**—The recent literature contains the reports of many studies of an acute condition involving both the brain and spinal cord, sometimes of undeterminable origin and sometimes following or accompanying acute infectious diseases or vaccination. A. A. Low (Arch Neurol and Psychiat. 23:696 (Apr.) 1930) made clinicopathological studies in 5 cases, all of which were children. The first case, aged  $2\frac{3}{4}$  years, had high fever, diarrhea, convulsions and coma, and died within 48 hours of onset. Autopsy revealed marked changes in the cells of the cortex—a process of liquefaction

The second case, aged  $5\frac{1}{2}$  years, had fever, headache and unconsciousness and died in  $3\frac{1}{2}$  days from the onset. There was bilateral Babinski. At necropsy the ganglion cells showed massive liquefaction in certain areas of the brain. In the third case, aged 5 weeks, there was irritability, drowsiness, generalized tonic and clonic convulsions and jaundice. The child was spastic and died 13 days after onset. Autopsy revealed a condition similar to the other two cases. A fourth case, aged 4 months, had vomiting, diarrhea, restlessness, irritability, elevation of temperature, rigidity of neck and spasticity of the extremities. A bilateral Babinski was present, with transient pupillary changes and ocular palsies. Death occurred in 12 days of onset. The ganglion cells showed vacuolation, neuronophagia and satellitosis. The fifth case, aged  $3\frac{10}{12}$  years, showed irritability, fever, retraction of head, mental dulness, jerking movements of eyes and bilateral Babinski. While in the hospital this patient developed, on the eighth day, an attack of measles and otitis media. Death occurred 39 days from onset. Autopsy showed swelling of ganglion cells of the cortex, vacuolation, neuronophagia, etc.

H. M. Zimmerman and H. Yannet (*Ibid.* 24:1000 (Nov.) 1930) report a case of measles in a boy of 4, who on the fifth day developed a sudden elevation of temperature to  $104^{\circ}$  F ( $40^{\circ}$  C.) associated with nausea, stiffness of the neck and later vomiting. Drowsiness, sphincter control loss, divergent strabismus, absent reflexes, positive Babinski and dysphagia were the outstanding symptoms which developed over a period of 6 days, at which time he died. The spinal fluid contained 90 to 135 cells, 90 per cent. being mononuclears. The pathology was characteristic of enceph-



alomyelitis—"a perivascular degeneration of the myelin of the white matter"

P Bassoe and R R Grinker (*Ibid* 23 1138 (June) 1930) studied a case of *rabies vaccination* who developed encephalomyelitis. The patient was a woman of 48 who had not been bitten, but had handled a rabid dog. She received 13 doses of 2 cc of serum, given on successive days. After the thirteenth dose she developed weakness of the legs, followed the next day by paralysis of the legs and retention of urine. Gradually there developed weakness of the arms and respiratory distress, with elevation of temperature to 103° F (39.4° C). The mind was clear and sensation normal. All tendon reflexes were lost. With gradually rising fever and other complications, she died about 1 month after the onset. The postmortem examination revealed extensive cell changes and "perivascular round cell infiltrations with demyelination and axis cylinder destruction." They also reported a case with the "typical clinical syndrome of rabies 1 year after a dog bite, beginning 2 weeks after a trauma to the bitten hand." The pathological findings were typical of rabies (negri bodies in the ganglion cells) and encephalomyelitis. These writers conclude that the vaccinal lesions represent an attenuated rabies virus disease, transmitted by the vaccine.

G B Hassin and J C Geiger (*Ibid* 23.481 (Mar) 1930) report their studies on a case of *postvaccinal (cow-pox) encephalitis* in a boy aged 7, who died about 2 weeks after the vaccination. On the eleventh day after vaccination he complained of severe frontal headache and became bedridden. He had convulsions and lockjaw the following day. His head was retracted, the upper extremities spastic, but tendon

reflexes were normal. The tentative diagnosis was tetanus and he was given serum. That night he had convulsive twitchings of the upper half of the body, slight temperature elevation and the jaws remained firmly closed. On the following day the temperature was 107.7° F (42° C), pulse 168, and respiration 68, 26,000 leukocytes, negative spinal fluid, he became stuporous and died that evening. The principal pathologic feature was the extra-adventitial glia cell infiltration, probably as a reaction to a local nerve destruction, while the adventitial or so-called perivascular infiltrations were insignificant and practically devoid of hematogenous cells. The changes, according to these writers, may be considered an acute stage of what is commonly seen in subacute or protracted toxic conditions of the brain. The authors emphasize the specific features of postvaccinal encephalitis: a definite incubation period (about 11 days), a rapid course, and recovery without sequelæ in about 50 per cent of cases. They state that the exact cause is not known, but histologic studies show that the most probable cause is not an infection, but some toxin which is occasionally too virulent and is contained within the vaccine lymph.

Encephalomyelitis in measles, which has attracted considerable interest, is discussed by A. Ferraro and I. H. Scheffer (*Ibid* 25 748 (Apr) 1931) who report 6 cases pathologically. The picture was the same in all cases, mainly a perivascular demyelination, with involvement of axis cylinders. The absence of hematogenous elements in the infiltrations causes the authors to doubt an inflammatory reaction and to favor a degenerative process (which they prefer to term an encephalopathy rather than an encephalitis).

H M Zimmerman and H Yannet (*Ibid* 26 322 (Aug) 1931) present the history and findings in a girl of 13 months who, on the third day following the appearance of an extensive varicella exanthem, became feverish, irritable and restless. On the following day there occurred 2 generalized convulsions. The child died during a third convulsion that night. The necropsy observations showed degenerative lesions of the ganglion cells of the brain and cord, with perivascular destruction of myelin sheaths in certain areas. In addition, there were small focal hemorrhages in the cerebral cortex.

### ENDOMETRIUM, HYPERPLASIA OF.—ETIOLOGY.—

The nature of hyperplasia of the endometrium is that of an overgrowth of its constituents, both epithelial elements and stroma. The endometrial overgrowth is evident on gross examination, revealing a definitely thickened mucosa as much as a 1.5 cm. in diameter. When the process is pronounced, the endometrium is thrown into folds which may form polypoidal protrusions into the uterine cavity, the condition then being called polypoid endometrial hypertrophy. The proliferative activity of the epithelial elements as well as of the stroma constitutes the characteristic feature of a more or less distinctive histological picture with slight individual variations. The stroma is excessive in amount and shows an abundance of cellular elements. The blood-vessels are often distended, with occasional extravasations of blood.

The glands, however, give the most specific histological feature of this condition. They are increased in number or densely crowded, and in most instances enlarged. They are lengthened

and tortuous but never invade the myometrium. Dilatation of these glands is common, cystically dilated glands being found chiefly in the middle zone of the endometrium forming the so-called "swiss cheese pattern."

The glandular epithelium is of the high columnar type with no suggestion of secretory activity. At times it presents a double row of elements, which occasionally may resemble the conditions found in the beginning of an adenocarcinoma.

J Hofbauer (*Surg Gynec Obst* 52 222 (Feb) 1931) observed that in guinea-pigs treated parenterally with derivatives of the anterior pituitary, conditions may be produced in the uterine mucosa, as well as in the ovaries, which are practically identical with those observed in endometrial hyperplasia in women. He suggests that hyperplasia may reasonably be regarded as the manifestation of an overactivity of the anterior pituitary lobe. The application of x-rays to the pituitary may be of value, therefore, in treatment of this condition.

C F Fluhmann (*Ibid* 52:1051 (June) 1931) found this condition present in 28 per cent of the last 1700 hospital admissions on the Stanford Gynecological Service. It accounted for 12.2 per cent. of a series of 507 women with abnormal uterine hemorrhage. The majority of cases were found just before and during the menopause.

The chief symptom is uterine bleeding, occurring either at cyclic intervals or continuous. The ovaries of these patients show cystic ripening follicles, atretic follicles and theca lutein cysts with an absence of mature corpora lutea.

Fluhmann refutes the theory of Hofbauer as to the origin of this condition. Functional studies revealed an excess

production of estrin. In only 1 of 10 patients was he able to find large amounts of anterior pituitary sex hormone in the blood. This suggests overstimulation of the endometrium by estrin as the possible etiological factor. Necrosis in the endometrium is responsible for the hemorrhage.

The etiology of this disease is as yet obscure but it is evidently the result of an *endocrine disorder* rather than a local pelvic condition. Repeated curettages in *younger patients* and *intrauterine radium* applications for *older women* are recommended as the best modes of therapy.

**ENDOPHTHALMITIS.**—To the 3 cases of destructive purulent ophthalmia accompanying eruptive fever with stomatitis, reported in the literature, J. M. Wheeler (Am J Ophth 13 508 (June) 1930) adds another case which occurred in a Jewish boy, aged 8, who developed ulceration and perforation of both corneae and panophthalmitis. After 3 months the vision of 1 eye was reduced to light perception and the other was blind.

**ENDOSCOPY.**—Endoscopy, including laryngoscopy, bronchoscopy, and esophagoscopy by the direct method, is assuming its just place as a diagnostic aid in the diagnosis and treatment of disease. Its value in the removal of foreign bodies has long been recognized but, with the advent of iodized oil (*radiopaques*) for the demonstration of lesions of the respiratory tract, this procedure is now one of the outstanding contributions to diagnostic medicine. Recent literature is full of reports from clinicians who are employing this method and the mass of evidence collected is of utmost value to the future usefulness of

this new method, *i.e.*, *bronchography*. While various opaque substances have been used by others, Sicard and Forestier (1922) were the first to introduce lipiodol.

It may be said that the practice of introducing radiopaque substances into the bronchi for diagnostic purposes is now thoroughly established. Many different methods have been employed to introduce these various contrast media into the tracheobronchial tree. Jackson, Clerf, Ballou and other bronchoscopists prefer the *bronchoscope* for this purpose, some favor the *transglottic method* of introduction, others the *laryngeal cannula* or *rubber catheter* placed into the larynx under indirect laryngoscopy, excellent results are also reported by introducing the material *supraglottically*, after cocaineization of the pharynx. A method of choice with some workers is the injection, with a specially made needle, into the *cricothyroid membrane*. Recently, S. Iglauer (J A M A. 97 1517 (Nov 21) 1931) described his ingenious modification of an *intubation cannula*, which is inserted into the larynx and through which the contrast media may be introduced. The author offers this method for the reason that bronchography has not been so generally adopted in children because of the difficulty of obtaining their cooperation. While ordinary x-rays of the chest are of great diagnostic value, there are many lesions which can be visualized with greater certainty and clarity after the introduction of opaque substances. The best medium for this purpose is a 40 per cent *iodized poppy-seed oil* (lipiodol). Such material is invaluable for visualizing the approximate shape, number and size and distribution of areas that occur in **bronchitis, pneumonitis, bronchiectasis, tuberculosis,**

asthma, and lung abscess. Notably, too, by repeating such observations, progress of the disease may be studied

While the injection of oil may be looked upon as practically free from danger or serious after-effects, bronchography is *contraindicated* in the presence of *high fever, dyspnea, recent hemoptysis, in cardiac decompensation and in cachectic individuals*

Regarding the indications in **tuberculous individuals**, Louis H Clerf (J A M A 97 87 (July 11) 1931) groups his cases into 2 classes for the purpose of discussion, *vis*, proved cases of pulmonary tuberculosis that develop certain symptoms or signs requiring investigation or treatment and cases which present obscure pulmonary signs suggesting tuberculosis, but in which the diagnosis cannot be established by the ordinary methods of examination, or unsuspected cases of tuberculosis that are diagnosed in the course of a routine bronchoscopic study. His case reports described a wheeze due to stenosis of a bronchus, an urgent dyspnea resulting from stenosis due to a fungating mass of granulation tissue. In the case of a massive lesion, as shown in the x-ray picture, in the lower lobe of the lung, with relatively little change elsewhere, Clerf was able to demonstrate the presence of marked bronchiectasis. In the group of unsuspected pulmonary tuberculosis cases this same author was able to demonstrate tuberculous pulmonary abscesses, rupture of tuberculous glands into the bronchi, tuberculomas and tuberculosis of the bronchial wall. He feels that hemoptysis does not contraindicate bronchoscopy unless the blood loss is great and continuous. Obscure hemoptysis should be an indication for bronchoscopy. Clerf feels that absolute *contraindications* are rare consider-

ing only *pneumothorax, extensive pulmonary involvement and laryngeal involvement*. In determining the contraindications, the importance of the indications should be considered, because no ill effects have been noted from bronchoscopy itself. The value of the procedure, enhanced by the use of the radio-paques, cannot be overemphasized in the differential diagnosis of pulmonary lesions.

As to the value of endoscopic methods, C Jackson (New England J Med 199 759 (Oct 18) 1928) ably sums up the situation as follows:

1 *Endoscopy for Research*—Endoscopy has greatly facilitated the study of pulmonary physiology and pathology. It affords a mechanical means for the placement of materials, inert as well as infectious, in the lungs and of observing the local as well as the general effect produced.

2 *Endoscopy for Foreign Bodies*—This represents today only about 2 per cent of the endoscopic examinations performed. The other 98 per cent are for the diagnosis or treatment of diseases.

3 *Endoscopy for Disease*—In all diseases of the larynx, trachea, bronchi, pulmonary parenchyma, mediastinum, hypopharynx, esophagus, and stomach, *direct vision, biopsy, and direct therapeutic or operative measures* have been added by endoscopic developments to the resources of the physician and surgeon.

Among accomplishments in diagnosis and treatment is direct laryngoscopy. Formerly it was impossible to look at the larynx of a baby.

*Bronchoscopic aspiration* of suppurative foci, which can be drained through the mouth harmlessly and without general anesthesia, is now possible. It is

the author's opinion that the fundamental factor in all pathological conditions of the lungs is impairment of the defensive power of the lung, due to impairment of drainage and aeration. By *bronchoscopic drainage*, the load is taken off the cilia and spontaneous drainage is established. With the restoration of aeration and spontaneous drainage, the defensive power of the lungs is re-established.

In the treatment of **pulmonary suppuration following tonsillectomy**, bronchoscopic aspiration is the method of choice in the incipient stage.

Since bronchoscopic studies have revealed the cause of a fatal form of **septic bronchitis** due to vegetable substances, especially the peanut kernel, it is now possible to prevent this condition.

In **spirochætosis** and **Vincent's infection**, the diagnosis of bronchial involvement is made from uncontaminated specimens removed from the bronchi through the bronchoscope.

In many cases of supposed **asthma**, the bronchoscope has revealed some form of mechanical obstruction of the bronchi. Hence the author's aphorism, "*All is not asthma that wheezes*."

The mechanism of **postoperative massive collapse of the lungs** was discovered by Lee and substantiated bronchoscopically by his coworkers. This condition is due to obstruction of a bronchus by viscid secretions. Kolmer found that the coagulation of the pus is due to an excess of fibrin. It is assumed that an excess of fibrinogen from passive congestion produces excessive viscosity. The viscid secretion can be aspirated with the bronchoscope. The result is usually prompt expansion of the lung. Coryllos and Bernbaum have demonstrated that **pneumonia** is essentially an atelectasis due to obstruction

of the bronchus by a thick exudate and hence relievable by bronchoscopic aspiration.

4 *Education of the Undergraduate*—The student is instructed regarding the symptoms, diagnosis, prognosis, and prophylaxis of foreign bodies in the air and the food passages, but receives no training in the technic of bronchoscopy.

5 *Education of the Graduate*—The technical difficulties of endoscopy and the methods of doing it along the systematic lines that have proved satisfactory are being offered in the larger post-graduate schools.

6 *Education of the Public*—Civic organizations are being used to educate the public in prophylaxis. Such instruction will prevent about 85 per cent of the cases of foreign body in the air and food passages and 90 per cent of the cases of **lye stricture**.

#### ENTROPION.—TREATMENT.

—Wendell L. Hughes (Am J Ophth 14 34 (Jan) 1931) reports effective and permanent relief of spastic entropion by the simple procedure of injection of 95 per cent alcohol into the outer fibers of the orbicularis muscle near the margin of the lower lid.

**ENURESIS. — ENURESIS IN CHILDREN.**—Every case of enuresis, according to C. Pototzky (Am J Dis Child. 40 46 (July) 1930), is merely the representation of a symptom, in many cases enuresis will be the expression of some neurosis. In other cases in which the patients are suffering from disturbances in intellect, the enuresis symptom will be the outward expression of one particular form of disturbance among many.

**ETIOLOGY. — Predisposing Causes.**—If there is any variation in

incidence of the condition in the 2 sexes, enuresis occurs more commonly in boys than in girls. S. J. Usher (Canad M A J. 24 665 (May) 1931, also F. N. Anderson (Am J Dis Child 40 591 (Sept), 818 (Oct) 1930). According to Anderson, neither *race* nor *color* are factors of appreciable importance. Mental deficiency seems to be a factor only in a small group of patients, since the intelligence of enuretic children is, on the whole, above the average. The time of *development* of certain fundamental processes such as dentition, walking and talking, the *height-weight ratios*, *left-handedness*, *tantrums*, *thumb sucking*, *aggressiveness* and *gregariousness*, and *masturbation* do not seem to be causative factors of enuresis. However, Pototzky (*loc cit*) contends there are certain types of cases in which a relationship between masturbation and enuresis cannot be denied. While this author also maintains that *deep sleep* may be a causative agent of enuresis, Anderson states that it is an observation so inconstant as to warrant no such conclusion. *Nail biting*, according to Anderson, occurs in a high proportion of enuretic children, and appears to be an outlet for emotional energy arising from mild adjustment from enuresis. *Feelings of inferiority* are extremely common in such children and while commonly not causal, yet, having developed, lead to the continuance of enuresis.

B. A. Thomas and R. J. Hubbell (J Urol. 26 107 (July) 1931) group the causes of enuresis under 3 headings: (a) pathology of the urinary organs, (b) disturbance of the reflex arc, (c) disturbance of cerebral control.

*Emotional factors* constitute by far the largest group of elements in the causation, or at least, the continuance of enuresis, according to Anderson (*loc.*

*cit*). Most contributory factors exert results on this basis. Although previous *illnesses* are factors of real importance in a large number of cases, yet they act mainly through relaxation of habit training rather than as a direct result of the illness. *Habit training* is one of the most important things to be considered as responsible for persistent enuresis. The *conditioned reflex* seems to account for many otherwise unexplained cases of enuresis. *Infantile traits* appear to be of high incidence among enuretic children.

Relationships between enuretic children and siblings are clearly etiologic to some extent in no small number of instances. Jealousy is perhaps the most common observation in this connection. Parental maladjustments occur with extreme frequency as products of emotional upsets in children and occurred in the families of two-thirds of all children studied. *Parental attitudes*, particularly those of "failure" and "severity," exert deleterious effects on measures for the control of enuresis.

**ONSET.**—According to Anderson (*loc. cit*), in about 80 per cent of all cases the onset was from infancy, representing the persistence of a once "normal" habit. In about 28 per cent. of the cases the onset was at some time following complete control of the bladder.

**TYPES OF ENURESIS.**—Ordinarily enuresis may be classified as *nocturnal*, *diurnal* or *combined* nocturnal-diurnal. In approximately four-fifths of all cases studied, Anderson (*loc cit*) found the purely nocturnal type. About 11 per cent. were of the combined nocturnal-diurnal type, less than 3 per cent were of the purely diurnal enuretic group. Seven per cent had combined enuresis and soiling.



Pototzky (*loc cit*) suggests the following grouping of different forms of enuresis

(1) *Neuropathic children* (especially those with vasoneurotic signs)

(2) *Psychopathic children* (with disturbances of power of volition) (a) defiant, unstable, (b) shy, timid, (c) indifferent, phlegmatic

(3) *Fetaltistic children*

(4) *Pathocrinal children* (a) in the sense of hyperthyreosis, (b) in the sense of hypothyreosis

(5) *Children disturbed in intellect, and epileptic subjects* (without manifest endocrinal components)

L Mandel (Brit J Child Dis 28 1 (Jan-Mar) 1931) has attempted to classify children with enuresis into the following group

(1) Those in whom some "palpable" physical irritating stimuli exist, *i e*, worms, overdistention of bladder, congenital malformations, cystitis, etc

(2) The hypersensitive, neuropathic or "nervy" type, in which the instability is a symptom which may be regarded in the same light as other symptoms, such as cyclic vomiting, ketonuria, vagotonia, etc, which are more commonly found in the "nervy" child

(3) The so-called psychopathic child, in whom the enuresis is more a behavior complex

(4) Endocrine dysharmony, particularly hypothyroidism, leading to a loss of inhibition.

(5) The debilitated child, often convalescent from some illness

*Physical irritating factors*, Mandel believes, have little or no relationship to enuresis. On the other hand, according to Thomas and Hubbell (*loc cit*), it seems quite significant that in almost one-half of the cases in the male, there was an enlarged or diseased *verumontanum*,

and *phimosis*, *malnutrition*, *hydroureter* and *hydronephrosis*, *granular urethritis* and *cystitis*, and *spina bifida occulta* were present often enough to warrant special mention. Of a group of 19 patients with enuresis reported by J Jacobovici, C I Urechia and E. Teposu (Presse méd 37 1103 (Aug. 24) 1929), 16 showed a small depression at the base of the spine which on x-ray examination was found to be associated with a *spina bifida occulta*. The remaining 3 cases of enuresis were due to other *osseous defects*. B Z Cashman (Am J Surg 8 558 (Mar) 1930) reported a case of enuresis in a 16-year-old girl due to the opening of an *aberrant ureter* into the vestibule of the vagina. Only a small amount of urine escaped through the aberrant ureter.

The patients with the *neuropathic* type of enuresis are hypersensitive in the broadest sense of the term and respond to every instance of unusual excitement in the form of a reflexive disturbance of the mechanism of the bladder. The simplest reflex, Pototzky states, is that resulting from exposure to cold air. There is also the mechanism of the *conditional reflex* to be considered. According to Mandel, many patients of this type show other evidence of hypersensitiveness, such as nail biting, stammering, vasomotor disturbances, blushing easily, etc. Mandel (*loc cit*) contends that it is into this class of the neuropathic child that most of the cases of enuresis fall.

In the psychopathic group Mandel places the *timid*, the *depraved*, the *phlegmatic*, *lazy*, and *dirty* child, *i e*, the psychologically abnormal child. According to Pototzky, this group is composed of several varieties or types of children. There is the type of child who, from severe fright, wets the bed

more frequently than ever. In another group is the child who is absolutely indifferent to the disturbance, and seemingly fails to understand what the reproaches are about. There is still another class of patients belonging to the group who wet the bed out of spite. There is yet another type in which the inferiority complex plays a part.

The *fetalistic* enuretic children are those whose development has remained dysharmonious. In children of this type, enuresis is not an isolated symptom. Pototzky (*loc cit*) describes 2 types of *pathocrimal* children, *ie*, *hyperthyroid* and *hypothyroid*. In children with hyperthyroidism it is not uncommon to find a condition of enuresis, especially in girls. It would appear that this may account frequently for the sudden onset of enuresis in prepuberty. In the hypothyroid group may be included the cases of enuresis with myxedema, and also of mongolism with a myxedematous component.

Enuretic patients with *disturbed intellect* and epileptic subjects without endocrinal derangements constitute the fifth group of Pototzky's classification.

The fifth group of Mandel's classification is not a true division of enuresis, but since enuresis is so often seen in *debilitated* children, the author ventures to classify these children in a distinct group.

**TREATMENT.—Organic Factors.**—Thomas and Hubbell (*loc cit*) emphasize that while the psychic factor is undoubtedly an important one, yet organic trouble must be looked for and corrected if present. According to Mandel (*loc cit*) only 10 or 15 per cent. of the cases of enuresis are cured by removal of possible irritating physical stimuli. Thomas and Hubbell recommend **fulguration** with a Bugbee

electrode in the local treatment of these patients with diseased *verumontanum* and *polypi*. J. Iacobovici, C. I. Urechia and E. Teposu (*loc cit*) treated 15 patients with *spina bifida occulta* by means of **extra-intradural resection**. Nine of the group were cured of enuresis by operation, 3 were relieved, 1 received gradual relief, and 1 showed no improvement, while 1 died. B. Z. Cashman (*loc cit*) successfully treated a case of enuresis due to an *aberrant ureter* by *ligating the ureter*.

**Neuropathic Child.**—Hypersensitiveness is rooted in the whole system of the neuropathic child. Exaggerated methods of arousing are harmful, as the sudden start accompanying the awakening will unduly excite the already agitated mechanism of the bladder. The aim of the treatment is to secure peaceful rest, either by light, harmless sedatives, or, in pronounced vasomotor cases, by endeavoring to correct the defective vasomotor process. According to Pototzky, **camphor** has a favorable regulating effect on the circulation; it also acts as a sedative in contractions of the bladder. This author usually prescribes some form of calcium in combination with camphor. For example, 0.1 Gm ( $1\frac{1}{2}$  grain) of **monobromated camphor**, and 1 Gm (15 grains) of **calcium lactate**. One powder should be taken at bedtime or twice a day. In the neuropathic group, as well as in all cases of enuresis, Mandel considers **atropine** or **belladonna** as the specific drug of choice. Atropine is the only drug in which R. K. Rewalt (Pennsylvania M. J. 33:386 (Mar) 1930) has any confidence. A 1:1000 solution is used with ascending doses to the point of tolerance and stopped just short of that point. For diurnal and nocturnal enuresis, the doses are administered at

10 A M and 3 and 7 P M For the nocturnal type, doses are given at 4 and 7 P M The maximum dose, usually  $\frac{1}{400}$  to  $\frac{1}{100}$  grain (0 00016 to 0 00065 Gm), is generally maintained for a period of from 2 to 6 weeks, after which it is gradually reduced The action of the treatment does not seem to be a psychic one, since in several instances, when the patients were doing well under atropine therapy, the substitution of water for atropine resulted in a return of the symptoms, the relapse quickly subsided when atropine therapy was resumed

S J Usher (*loc cit*) used the **psychic treatment** in all his cases of enuresis This treatment consisted in injecting 1 c c (16 minims) of sterile, distilled water once a week, at which time the child was assured that this treatment would result in a cure He is warned, however, that should a relapse occur, additional injections would be administered However, in the case of the high-strung and nervous child, **luminal** was also administered In most cases where psychic and luminal therapy failed, **atropine** was used The author concluded that psychic therapy is a valuable addition to the general measures employed in enuresis and that those cases not improved by these measures could be greatly relieved or cured by administering atropine and luminal, alone or together

Pototzky has failed to see that electrical treatment of the vesical region of the bladder produced beneficial results although it has been advocated by some He *warns against the use of epidural injections*, pointing out that they are not without danger The use of hydrophathic measures in the treatment of patients with enuresis might result in ill effects on account of association of water and bed-wetting, on the other hand,

there is much that is good in **air baths** for most neuropathic, enuretic children

**Psychopathic Child**—In the treatment of children of this group Pototzky states that abnormal *deep sleep* is often observed which is described by some authors as pathognomonic of enuretic patients and just as often denied by others Medically, **camphor** is said to be the only therapy likely to be of any value Above all, in cases of this type the “**awakening**” therapy, usually at 11 P M is an absolute necessity These are the children who during the day can be trained to control the action of the bladder by special exercise such as willfully holding back the urine Here, too, the **suggestive treatment** is of value The child is made to say every evening aloud “I will keep dry” It goes without saying that these children should be encouraged by approval rather than discouraged by disapproval

**Fetaliatic Child**.—General speaking, the treatment consists in administering **calcium**, **vitamines** and general **roborants**.

**Pathocrinal Child**—In the case of female patients with hyperthyroidism, **ovarian preparations** are of use In the hypothyroid patient, the treatment is essentially that for hypothyroidism in general

**Patients with Disturbed Intellect; Epileptic Subjects**.—These patients, according to Pototzky are especially difficult to deal with In general, the treatment consists in persistent, untiring training.

**ENURESIS IN WOMEN.—SURGICAL TREATMENT.**—M. K. Smith (Ann Surg 92 394 (Sept) 1930) discusses the surgical treatment of this most annoying condition Urinary incontinence may be due to relaxation or rupture of the internal vesical

sphincter Under ordinary circumstances these women have perfect control of the bladder but become incontinent following excessive excitement or exertion Smith advocates a careful plastic repair of the anterior vaginal wall to correct the loss of bladder control In severe cases best results are obtained by the Kelly operation of tightening the vesical sphincter, together with a colporrhaphy

In one case where this failed, he obtained a cure by affording suprapubic bladder drainage to the plastic on the sphincteric area supplemented by an interposition operation From the standpoint of the urologist, suprapubic bladder drainage is a minor addition to any operation, whereas the rest it affords the bladder may spell success for the operation.

**EPIDERMOPHYTOSIS.—TREATMENT.**—The remedies employed in the treatment for epidermophytosis are almost as numerous and various as the authors who have written on the subject, and according to S Ayres, Jr., N. P Anderson and E. M Youngblood (*Arch Dermat and Syph* 24:283 (Aug) 1931), but little improvement has been made over the application of Whitfield's original ointment, one formula of which is as follows:

R <i>Salicylic acid</i>	gr xxx (2 Gm)
<i>Benzoic acid</i>	gr lx (4 Gm)
<i>Benzomated lard</i>	3j (30 Gm)

Almost without exception, patients with the condition are not advised regarding sterilization of their shoes, stockings or floor It has been shown that spores of epidermophyton may remain viable on the ground as long as a year or more It is difficult, therefore, to see how a permanent cure can be ex-

pected in this disease if the patient is merely given an ointment and not instructed in regard to preventing recurrences It is a comparatively simple matter to relieve the patient in an attack by prescribing any one of a number of suitable remedies, but without adequate sterilization of shoes, stockings, bath mats and bedroom and bathroom floors, subsequent attacks, as well as a spreading of the disease to other members of the family, are almost inevitable

Even though socks can be boiled for a prolonged period, shoes and floors cannot be subjected to this treatment, and discarding the shoes still leaves the floors to spread the infection Anti-septic solutions and disinfectants are difficult to apply to carpeted floors Some country clubs have adopted the use of paper slippers (Sanitreads) for protection against the bare floors

Fumigation with a formaldehyde candle is a simple and effective method of sterilizing all of the materials with which the infection has come in contact The following experiment was undertaken to determine the effectiveness of this procedure

The susceptibility of 3 of the more common types of pathogenic fungi to the fumes of formaldehyde was studied: *Epidermophyton* (Kaufman-Wolff), *Monilia albicans* and *Microsporon lanosum* In each instance, fresh material from active lesions, as well as dried material from old cultures, was used The material to be sterilized was placed on the floor of a room approximately 9 by 12 feet, and corresponding material was planted on fresh tubes of Sabouraud's medium as controls. Before placing the formaldehyde candle in the room, hot water was allowed to run into a basin for 10 minutes to increase the humidity of the room, since the fumes

penetrate more rapidly in the presence of moisture. The same result could have been attained by having a basin of steaming hot water in the room before and during the fumigation. The windows and doors were closed and the cracks stuffed with paper. The candle was then lighted and the room kept closed for 4 hours. At the end of the period the samples of material were planted on fresh tubes of Sabouraud's medium, and these and the controls were allowed to remain in a dark closet at room temperature. Growth took place in each of the control tubes within from 4 to 10 days, but all of the tubes containing fumigated material remained sterile.

The following table illustrates the results of the experiment.

Organism	Source of Material	After Exposure to Formaldehyde Fumes	Controls
Epidermophyton	Scales from infected foot 11-months-old culture	No growth in 43 days No growth in 43 days	Pure culture in 4 days Pure culture in 4 days
Microsporon lanosum	Infected scalp hairs 11-months-old culture	No growth in 43 days No growth in 43 days	Pure culture in 7 days Pure culture in 7 days
Monilia albicans	Scales from mouth lesions 9-months-old culture	No growth in 43 days No growth in 43 days	Pure culture in 10 days Pure culture in 6 days

**Comment.**—In the practical application of this procedure, patients should be instructed to place all of their shoes, slippers, athletic shoes, socks, stockings, bath mats and any other material coming in contact with their feet, in the bedroom or bathroom and to fumigate both rooms. It is preferable to fumigate once about 1 week after the patient has begun the use of an antiparasitic remedy locally, and once more after he is clinically and microscopically free from the disease. In cases of active infections of the hands or crotch, the gloves, golf-clubs, underwear, athle-

tic supporters, etc., should be fumigated, and in cases of ringworm of the scalp, all hats, combs, brushes, etc.

No remedies, especially local remedies that are excessively irritating, should be employed for an indefinite time. The type of medication commonly employed for fungus diseases is necessarily irritating, and, if used injudiciously, an eczematous condition may be substituted for the original infection. Microscopic examination of scales macerated in 40 per cent potassium hydroxide should be made prior to the institution of treatment and at intervals until organisms can no longer be found. Intermittent treatment for about 2 weeks after the skin is microscopically and clinically well, combined with fumigation, as has been described, besides careful attention

to infected toe-nails, which may act as a focus of reinfection, should give a considerably higher percentage of permanent cures than is commonly obtained.

**EPILEPSY.**—The literature on the convulsive states, particularly epilepsy, has been voluminous during recent years. Newer methods of investigation, as well as more extensive knowledge of physiochemistry, have undoubtedly been in a measure responsible for this increased interest and activity. No facts unearthed up to the present time, however, have settled the question of the

etiology and mechanisms of epilepsy. Each intensive study has contributed something, even though it may be on the negative side by eliminating one more factor or possibility.

**ETIOLOGY.**—L O Morgan and C A Johnson (Arch Neurol and Psychiat 24 696 (Oct) 1930) reported on the production of convulsions by experimental lesions of the tuber cinereum in animals. For purposes of orientation the tuber cinereum or postchiasmatic eminence is a relay station in the gustatory tract, situated just behind the optic chiasm, and including the bulbus infundibuli, the infundibular stalk of the pituitary and the eminentiæ laterales. It is in front of the mammillary bodies and the third ventricle lies above it. It contains several nuclei and tracts of fibers, whose functional significance are not clearly known.

As a result of experimentally produced lesions (injections of mercuric chloride) in this area, the authors summarize their findings somewhat as follows. The animals were normal in appearance, but developed periodic convulsions. Seizures began 2 to 6 hours after operation and were characterized by disorientation, dilatation of pupils, salivation, vasoconstriction, increased heart beat, muscular spasms of the face, jaws and anterior part of the body. Convulsions increased in frequency and severity, with typical tonic and clonic characteristics, followed by unconsciousness. Status epilepticus developed, usually resulting in death. The author noted several blood chemistry studies, but drew no deductions therefrom.

From the side of the *chemical* causes of epilepsy experimentalists have used various substances, such as picrotoxin, camphor, monobromata, absinthe, etc. F H Pike, C A Elsberg, W. S Mc-

Culloch and M N Chappell (*Ibid* 23 847 (May) 1930) employed the latter convulsant on cats by the intravenous route, noting clonic and tonic manifestations in the skeletal muscles, respiratory effects and various autonomic responses. Repeating the injections of absinthe after the removal of one cerebral hemisphere, tonic convulsions occurred on the side controlled by the removed hemisphere, and clonic movements on the well side. It would seem from this evidence that it might be inferred that the cortex is responsible for clonic convulsions and the extrapyramidal system for tonic convulsions. Another experimental approach to the same question was made by cutting off cerebral circulation until a severe anemia had been effected. In such animals the injections of absinthe caused only tonic convulsions. The authors conclude: "(1) Clonic convulsions arise from the cerebral motor cortex when this is anatomically and functionally intact. (2) Tonic convulsions arise from the lower motor mechanisms, in the period immediately succeeding an injury to the cortical motor mechanisms. After the lapse of sufficient time, clonic responses may be elicited from them. This is, however, not evidence that clonic convulsions may and do arise from the lower motor mechanisms when the cortical mechanisms are intact. (3) Tonic convulsions are absent in the early post-operative stages in animals in which the midbrain has been split longitudinally in the median line, while clonic convulsions persist if the pyramidal system is intact. (4) All parts of the motor mechanism act together as one system when the brain is intact. It does not seem probable that when the whole motor system is intact one part of the mechanism gives rise to movements of



one type and some other part of the mechanism independently gives rise to movements of another type "

W G Lennox and M B Allen (*Ibid* 23 521 (Mar) 1930) studied the *sugar content* of the spinal fluid in epileptics to determine if any relationship existed between convulsive seizures and the percentage of sugar. They compared the blood and spinal fluid sugars in 113 patients and found the ratio to be normal. Another study by the same authors was made (*Ibid* 23 525 (Mar) 1930) with regard to the chloride content of the blood and spinal fluid and from an examination of 120 patients they concluded that the average value for chloride in the blood and in the spinal fluid and the ratio of chloride in the spinal fluid to that in the blood were within the limits of normal.

Monobromated camphor was used in experimental production of epileptic fits in cats and compared to the epilepsy of man by S B Wortis, H C Coombs and F H Pike (*Ibid* 26 156 (July) 1931) showing a very close parallelism and emphasizing the value of such a convulsant for investigative purposes.

*Water balance* as a causative agent in epilepsy has been considerably discussed. J L Gamble (*Ibid* 23 915 (May) 1930) studied the fixed base excretion and concluded that there is a disturbance of body fluid volume control in epilepsy. On the basis that "sodium makes up nearly all of the total fixed base contained in extracellular (interstitial) body fluids, . . . the body water thrown out during the periods of seizure is of interstitial origin." His studies were made on an epileptic patient of 11, who had 2 days of convulsive seizures alternating with intervals between of 4 to 7 days. With a constant diet he found that sodium was excreted in large quan-

ties during the periods of seizures, but comments that such findings may "be simply products of the convulsive state and are, therefore, without pathogenic significance." He found no evidence of intracellular water.

T Fay (*Ibid* 23 920 (May) 1930) has commented on the relationship of water balance to the convulsive state in a large number of publications and it is his belief that maintenance of proper balance prevents convulsions and is "effective when other means of treatment have failed."

W Spielmeyer (*Ibid* 23 869 (May) 1930) approaches the problem from the anatomic basis—and the probable pathophysiology. He concludes that *vasomotor disturbances* are effective in the mechanism of the epileptic attack—a vasomotor spasm. He distinctly believes in an association of vasomotor instability with epilepsy and produces careful histological studies and associated phenomena reported in other fields of medicine to support his contention. He does not state this as a cause, but as a mechanism.

As perhaps offering some support to the vasomotor instability concept of Spielmeyer, is the observation by J. M. Nielsen and E. L. Eggleston (J. A. M. A 94 860 (Mar 22) 1930), who found amongst other things, symptoms which might be called vagotonia and sympatheticotonia in 3 cases of functional dysinsulism, exhibiting convulsive seizures. Feeding various glandular substances, particularly **suprarenal extract**, caused a cessation of attacks for periods of a few weeks to nearly 2 years.

From the angle of *allergy* the study of epilepsy has received considerable attention, bringing to mind the bracketing of migraine, asthma, hay fever and epilepsy by some authors and investiga-

tors G L Waldbott (Arch Neurol and Psychiat 23 361 (Feb) 1930) reports 2 cases suffering from epileptiform convulsions that alternated with asthmatic attacks. He believes that the epilepsy was due to hypersensitivity and refers to many similar cases in the literature. The allergic manifestations may be asthma, hay fever, urticaria or angioneurotic edema. F A Ely (*Ibid* 24 943 (Nov) 1930) made a statistical study of heredity in migraine and epilepsy. He studied the case records of 104 subjects of typical migraine, 171 subjects of epilepsy, and 100 persons as normal controls. His conclusions are as follows: "(1) A constitutional tendency to the development of migraine is transmissible from parent to offspring. (2) A migrainous ancestral trend predisposes the offspring to epilepsy. (3) Ancestral epilepsy is a less important factor in predisposition to epilepsy in the offspring than has previously been believed. (4) There is a preponderance of evidence indicating some definite clinical relationship between migraine and epilepsy."

The occurrence of epileptiform convulsions with *brain tumors* is reported by H. L. Parker (*Ibid* 23 1032 (May) 1930). In 313 cases of intracranial tumors, 21.6 per cent were found in which major epileptic seizures had occurred. In all of these 67 cases the tumors were supratentorial, with the majority in the frontal, parietal and temporal lobes. Convulsions were the initial symptoms in 38 of the 67 cases, and in 13 cases no other symptom had been present for one or more years.

**PATHOLOGY.**—From the pathological standpoint, L. O. Morgan and H. S. Gregory (Am J Psychiat 9:805 (Mar.) 1930) examined the brains of 21 epileptics and found that the tuber cin-

ereum had undergone unmistakable changes of a degenerative type. Microscopic examination showed marked hyperemia and shrinkage of cells to a marked degree. The conclusion is reached that lesions of the tuber cinereum may have some etiological significance in epilepsy.

**TREATMENT.**—Each year brings a crop of new ideas for the treatment of epilepsy and finds an equal number again discarded. Until the anatomico-physiologico-chemical basis for this disease has been found, all treatment will necessarily be unsatisfactory. It is a hopeful sign, however, that despite perpetual discouragement, medicine still reaches out sincerely and earnestly for a "cure." It is interesting, however, to note the degree of success which is reported with each different type of treatment. For instance, C. J. Barborka (*Ibid* 23.904 (May) 1930) treated 100 adult patients with a ketogenic diet with the result that in 12 cases the attacks were controlled, in 44 there was definite improvement, and in 44 cases there was no change whatsoever. Waldbott (*loc cit*) reports 1 case of epilepsy with no convulsions for 1 year following the omission from his diet of foods to which he showed definite hypersensitivity.

Fay (*loc cit.*) reports the results of dehydration on 2 groups of patients, one group observed over a period of 2½ years and the other less than one year. He concluded that proper control of fluid intake, combined with dehydration, has greatly diminished the tendency to convulsive seizures. The generalized and stuporous phases of the attack have been relieved by dehydration. Dehydration has also proved to be a valuable adjunct in the control of major convulsive seizures and has been found to

be effective when other means of treatment have failed. Fay's method of procedure is somewhat as follows. The patient must be hospitalized for "careful check and observation," with a determination of intake and output of fluids under the patient's normal routine. At the end of the observation period an encephalogram is made and the patient starts off on the dehydration plan, with all the fluid removed that can be obtained from the central nervous system, through lumbar drainage. As a result of the air injection, the patients have terrific headaches for a day or two, during which time they have no desire for liquids and food—thus furthering dehydration by establishing a marked restriction of the "fluid level." After this, the patient is allowed 10 to 16 ounces (300 to 480 cc) of total liquid in 24 hours (unless his history shows many and severe attacks, in which case 10 ounces only are permitted). To relieve the very distressing *thirst* which the patient has this fluid is given in small doses, equally divided over the 24-hour period. Fruit juices are permitted, but are counted in with the other fluids. Chewing of gum and orange peel was found of value in relieving thirst.

In 10 days' time the dehydration brings about a definite establishment of the low fluid level without much further discomfort, according to Fay. It is admitted that many patients are very uncooperative and, therefore, difficult to keep on the extremely low level of fluid intake. The diet is adjusted carefully from the standpoint of water content and toast is given instead of bread, baked potato instead of boiled or mashed, and dry cereal instead of the cooked forms. The vegetables are drained of juices before serving, and sauces, juicy fruits and gravies are

avoided. Ice cream, candy and sweets are not permitted. Starches have been permitted to avoid acidosis. A saltless diet has been maintained to assist in the release of body fluids, the low salt diet also assists in the control of thirst. The aim is to keep the output slightly below the intake. Acidosis was not observed in any of Fay's patients and he warns against a ketogenic diet with dehydration, lest it precipitate a severe acidosis. On the other hand, Waldbott uses a definite restriction of fluids with his ketogenic diet.

As a result of dehydration, Fay reports in some cases lessening of irritability, improvement in memory and mental alertness, change in the character of seizures (lessening of duration of attacks and freedom from postconvulsive stupor, *ie*, rapid return of consciousness), disappearance of vomiting and headache, *petit mal* attacks replacing *grand mal* in some cases (although the reverse was noted in 1 case). In 14 cases followed for 2½ years, 4 were greatly improved, 2 were definitely improved, 2 were improved slightly, 3 were unimproved, and 1 was symptom-free with no attacks for a year and 10 months. In 8 cases followed less than one year, 2 were greatly improved, 3 were slightly improved, 1 was unimproved, and 2 were free from attacks.

Neilsen and Eggleston (*loc. cit*) reported 3 cases freed of attacks in 27 months, 18 months and 7 weeks, respectively, by the use of suprarenal extract in frequent feedings. These cases suffered from a functional dysinsulinism with epileptiform seizures.

#### ERGOSTEROL, IRRADIATED.—EXPERIMENTAL RESEARCHES ON THE ACTION.—

The antirachitic and calcifying proper-

ties of this preparation are discussed by H. Simmonet and G. Tanret (*Presse méd* 39 932 (June 24) 1931), and also a direct toxic influence which does not run parallel with the first quality, and whose relationship is not yet definitely established. They have proved that a moderate irradiation develops the antirachitic property to its maximum. Pushed a little farther, the irradiation does not vary the antirachitic property materially, but notably increases the toxic quality. The suggestion is advanced that this fact may account for certain accidents of intolerance in children when this preparation first came into use because of its having undergone too long a process of irradiation.

To develop the antirachitic property to a maximum and to reduce to a minimum the toxic factor, which accompanies the calcifying factor, presents a complex problem in the details of its execution, involving the elements of time of irradiation and degree of heat developed.

As to the integrity of the vitamin D element with regard to its keeping qualities, it was found that while not absolutely constant, it undergoes little change with time, and its activity remains practically unaltered in an ordinary bottle after the period of a year, at ordinary temperatures. It withstood for 15 minutes a temperature of 150° F. (65.6° C.) without its antirachitic or toxic properties being sensibly diminished.

Experimentation was practiced upon 150 rabbits, rats and guinea-pigs, the first mentioned being only less sensitive than the rat, while the guinea-pig was much higher in the scale of resistance to irradiated ergosterol. It was proved that rabbits were not affected by large doses of nonirradiated ergosterol given

daily and that no lesions were produced, particularly was this true as regards arterial atheroma.

It was sought to differentiate the calcifying quality and the toxic factor of the irradiated ergosterol, which occasionally appeared in surprising intensity.

The individuality of these 2 factors was apparently established by the fact that rabbits which received huge doses of the preparation daily (10 to 20 cc — 1½ to 3 grains) showed a rapid mortality, being killed by an obscure process, but without having calcification, without arterial lesions, and without glandular lesions visible to the naked eye. At the same time smaller doses developed an intense calcification of the arterial system. Thus, by the employment of these massive doses the process of calcification had not yet had time to manifest itself, for the toxic process had killed the animals by a process altogether different from that of calcification.

Descriptions of the lesions of calcification provoked by high doses of irradiated ergosterol and the histological studies of these conditions are referred to by the authors as having been published by other investigators. This process shows as an elective site the arterial system or, more exactly, its elastic fibers. There is a calcification of the aorta, sometimes as massive as an ossification. The efferent arteries are affected before the aorta. In rare cases the valves and columns of the heart itself are also involved. The veins are never affected.

With smaller doses of ergosterol it is possible to maintain alive calcified animals during a considerable lapse of time. The calcified arteries are not of themselves the cause of death, but 2 other lesions, *viz.*, renal calcification and

gastric hemorrhages, are responsible. The cortical zone of the kidney appears as a shell of calcification surrounding the medullary zone, which is much less affected. The stomach and, in a less degree, the duodenum present extensive hemorrhagic areas and necrotic zones—lesions probably due to the changes in the submucous arterioles. So long as the great glandular organs escape calcification, the animal will live in spite of the arterial calcification. It is not until the calcification blocks the vessels of the kidneys and stomach that the fatal cachexia develops. This fatal process may develop in a few weeks, 10 to 25 days, or sooner, in the case of an animal to which subtoxic doses of irradiated ergosterol are administered daily. It is not so much the case when interrupted dosage is practiced. If the doses are given 4 days per week, with 3 days of rest, the animal survives for many months.

The authors kept rabbits for a year which otherwise would have died in 30 days. The periods of rest seem to serve for detoxication, and in a certain measure for decalcification of the arteries. This is referred to as important from the viewpoint of human therapeutics and it is suggested that interrupted dosage may permit of larger doses and larger exhibition of the preparation.

*Iodide of potassium as a preventive of calcification* in high dosage of irradiated ergosterol proved remarkably efficient in some cases.

In controlled experimentation an animal who did not receive iodide of potassium succumbed in 7 months on a dosage which when given to another rabbit, who received at the same time iodide of potassium, inflicted no injury. The second animal at the end of a year was sacrificed for examination and showed

the aorta to be normal except for very slight calcification which only chemical analysis could demonstrate.

In the experimentation there occurred many times cases in which rabbits showed a resistance to doses which were fatal to the average rabbit. On doses which proved fatal generally in 15 to 20 days, these occasional rabbits showed an ability to survive for months. The authors account for this by considering that there exists a resistance to the preparation under consideration which aligns itself with the insulin resistance and arsenic resistance found in certain patients. Its cause, influence of race and diet, was not discovered, but the condition was repeatedly met with and necessitated the employment of many animals to arrive at clear results in the whole investigation.

As to the *source of the calcium* in the phenomenon of calcification, it was found that when the calcium deposit was small, the source was from without, being derived from the ingestion of food, and no change in the osseous parts occurred. When, however, the arterial calcification was particularly rapid and extensive, there was a true transfer of the calcium of the bones to the elastic tissue. The ribs became fragile, breaking like matches, and the large bones, such as the femur, showed themselves to be partially decalcified.

By subcutaneous injection of oily solution of the irradiated ergosterol, it was possible to cause the formation of calcareous plaques at the point of injection.

Some research was made concerning the influence of irradiated ergosterol upon gestation and the development of the young. A female somewhat resistant to irradiated ergosterol was given daily 5 mgm. ( $\frac{1}{12}$  grain) during

pregnancy until the birth of her young. The period of gestation was normal and resulted in the birth of 8 healthy individuals. The dosage to the mother was continued during lactation. These vigorous young ones were placed upon a rachitic diet along with another litter from an untreated mother as a control. These latter showed clearly the lesions of rickets, while the 8 former were resistant, and radiography did not show in them any characteristic deformity of the tibial heads.

The quantity of the factor vitamin D accumulated in them during the gestation and nursing periods afforded protection against later deficiency.

The authors believe that this demonstrates experimentally the value of *irradiated ergosterol administered to pregnant and nursing women, as a preventive against rickets in their offspring*.

Being in possession of an agent capable of producing calcification, the desirability of causing this process in a location where it might have beneficial results suggested its employment for calcification of tuberculous lesions of the lungs. An extensive study of this problem is described in the case of rabbits infected with pulmonary tuberculosis derived from bovine source, the most virulent type for the rabbit. Normal rabbits, normal rabbits treated with irradiated ergosterol, tuberculous rabbits, and tuberculous rabbits treated with irradiated ergosterol, were all put upon a dosage of calcium in the hope that the already known and demonstrated tendency of calcium to be collected at pulmonary and other tubercular lesions might be taken advantage of in effecting beneficial results. Although the calcium percentage in the lungs of these 4 classes of rabbits was raised quite high, and in the case of irradiated ergosterol

treated tuberculous individuals was raised as high as 5.5 and 14 per 100 pounds of lung (dried at 100°), all the infected animals died without the appearance of any arrest of the tubercular process.

The authors consider that this last series of observations apply particularly to the rabbit, an animal which is peculiarly susceptible to rapid tuberculosis, but do not limit at all the trials which might be undertaken in the more prolonged tuberculous processes of other species, man in particular, trials which need to be made boldly with rather large doses and interrupted administration, since it has been seen that high dosage with intervals of interruption avoid, in great measure, the calcification of the arterial system which is so dangerous.

**ERYSIPELAS OF THE STOMACH.**—Harrison S. Martland and David S. Eisenberg (Arch. Path. 8: 744 (Nov.) 1929) report a case of primary idiopathic phlegmonous gastritis of streptococcal origin which, on autopsy, was found to be a case of erysipelas of the stomach. In 1927, 263 cases of this disease had been recorded. It occurs between the ages of 20 and 60, and is about 3 times as frequent in men as in women. It may either be diffuse, extending over the entire stomach wall, or it may occur in localized patches.

According to Geister, the typical symptoms are sudden onset, profound prostration, high fever, chills, intense epigastric pain and tenderness, repeated severe vomiting and more or less rigidity. Peritonitis occurs in about 65 per cent of the cases.

It must be differentiated from acute gastric ulcer, acute pancreatitis, or acute



cholecystitis It is usually fatal, although recovery has been reported The average duration of disease is from 1 to 2 weeks and in a few cases death has occurred a few hours after onset With a possible single exception, phlegmonous gastritis has never been interpreted as erysipelas of the stomach

In 1 case reported the pathology was almost entirely confined to the submucosa and was characterized by extensive boggy edema The central areas showed the presence of abscesses and necrosis. The streptococcus present was found to belong to the group *Streptococcus erysipellus*.

**ESOPHAGUS.—CANCER.**—The importance of the problem of cancer of the esophagus has been mentioned by E. C Ernst (Ann Otol, Rhin, Laryng 40 870 (Sept) 1931) He states that from 6 to 10 per cent of the reported fatal malignancies occurred in this region. The seriousness of the problem is evidenced by the scarcity of 5 year cures reported. The author believes there are several reasons for this situation the lack of early diagnosis, due to the inaccessibility of the region, the difficulty of approach for surgical treatment; and the early extension of the lesions being among the most prominent

**Diagnosis.**—As a radiologist, Ernst suggests methods of early x-ray diagnosis Most important is a thorough examination by fluoroscopy as well as radiographically, using every conceivable position Observation should be made of the size, shape, outline and position of the esophageal lumen, the deglutition and peristaltic phenomena, and the degree of obstruction if present All suspected cases should be studied in the Trendelenburg position to outline the lower limits of involvement. The hori-

zontal position is also advocated by this writer Differentiation must be made from local irritation due to foreign bodies, localized ulcerations, simple tumors, polyps, and tuberculous and syphilitic infiltrations Cardiospasm often is difficult to differentiate, although characteristically the dilatation above the spasm is usually oval and has relatively smooth shaped round corners, as compared to cancer with its irregular margins

Chevalier Jackson (*Ibid* 886) emphasizes the fact that when a history of dysphagia, weight loss, pain, emaciation and cachexia is found, the lesion is usually hopeless Early diagnosis depends upon x-ray and esophagoscopy, with or without biopsy In Jackson's experience the positive x-ray diagnosis is correct in 90 per cent of cases, and a negative x-ray report is correct in 85 per cent From the esophagoscopist's viewpoint, there are 2 classes of cases (1) periesophageal growths, and (2) those that are endoesophageal by origin or extension The latter make up about 90 per cent of the cases in the author's clinic The early lesion "usually consists of one or more nodules covered with eroded epithelium, later the nodule ulcerates and fungations appear A fungating, bleeding ulcer is the type of lesion most frequently seen in the esophagoscope" In periesophageal growths, the infiltration is easily recognized "So long as the patient is allowed to drift on to death under erroneous inferential diagnosis of 'spasm' and 'globus hystericus,' just so long will it be useless to try to lessen the mortality of cancer of the esophagus"

**Treatment.**—As to treatment, Ernst (*loc cit.*) mentions the most common methods as being **gastrostomy, dilatation of the esophageal stricture**, with

pregnancy until the birth of her young. The period of gestation was normal and resulted in the birth of 8 healthy individuals. The dosage to the mother was continued during lactation. These vigorous young ones were placed upon a rachitic diet along with another litter from an untreated mother as a control. These latter showed clearly the lesions of rickets, while the 8 former were resistant, and radiography did not show in them any characteristic deformity of the tibial heads.

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In 1 case reported the pathology was almost entirely confined to the submucosa and was characterized by extensive boggy edema The central areas showed the presence of abscesses and necrosis The streptococcus present was found to belong to the group *Streptococcus erysipellus*

**ESOPHAGUS.—CANCER.**—The importance of the problem of cancer of the esophagus has been mentioned by E. C. Ernst (Ann Otol, Rhin, Laryng. 40 870 (Sept.) 1931) He states that from 6 to 10 per cent of the reported fatal malignancies occurred in this region. The seriousness of the problem is evidenced by the scarcity of 5 year cures reported The author believes there are several reasons for this situation. the lack of early diagnosis, due to the inaccessibility of the region, the difficulty of approach for surgical treatment; and the early extension of the lesions being among the most prominent

**Diagnosis.**—As a radiologist, Ernst suggests methods of early x-ray diagnosis Most important is a thorough examination by fluoroscopy as well as radiographically, using every conceivable position Observation should be made of the size, shape, outline and position of the esophageal lumen, the deglutition and peristaltic phenomena, and the degree of obstruction if present All suspected cases should be studied in the Trendelenburg position to outline the lower limits of involvement. The hori-

zontal position is also advocated by this writer Differentiation must be made from local irritation due to foreign bodies, localized ulcerations, simple tumors, polyps, and tuberculous and syphilitic infiltrations Cardiospasm often is difficult to differentiate, although characteristically the dilatation above the spasm is usually oval and has relatively smooth shaped round corners, as compared to cancer with its irregular margins

Chevalier Jackson (*Ibid* 886) emphasizes the fact that when a history of dysphagia, weight loss, pain, emaciation and cachexia is found, the lesion is usually hopeless Early diagnosis depends upon x-ray and esophagoscopy, with or without biopsy In Jackson's experience the positive x-ray diagnosis is correct in 90 per cent of cases, and a negative x-ray report is correct in 85 per cent. From the esophagoscopist's viewpoint, there are 2 classes of cases (1) periesophageal growths, and (2) those that are endoesophageal by origin or extension. The latter make up about 90 per cent of the cases in the author's clinic. The early lesion "usually consists of one or more nodules covered with eroded epithelium, later the nodule ulcerates and fungations appear A fungating, bleeding ulcer is the type of lesion most frequently seen in the esophagoscope." In periesophageal growths, the infiltration is easily recognized. "So long as the patient is allowed to drift on to death under erroneous inferential diagnosis of 'spasm' and 'globus hystericus,' just so long will it be useless to try to lessen the mortality of cancer of the esophagus"

**Treatment.**—As to treatment, Ernst (*loc cit*) mentions the most common methods as being gastrostomy, dilatation of the esophageal stricture, with

or without **radium** implantation, and the employment of external radiation by high voltage **x-ray**. He believes that gastrostomy should be limited to those cases showing marked obstruction, dilatation depends upon the type and location of the lesion, and in his experience radium implantation has not been a very advisable procedure in most instances. In all cases, whether radium is used or not, deep x-ray therapy is used by the author, in many instances with considerable success in decreasing involvement and symptoms.

Jackson (*loc cit*) believes **surgical treatment** is possible in many early cases. "The fundamental reason for the thousands of agonizing deaths from cancer of the esophagus is false education. The mind of the medical student and the medical practitioner is saturated with 3 erroneous ideas (1) that esophageal obstruction is often spasmodic, (2) that cancer of the esophagus is to be detected by obstruction to the passage of a bougie, (3) that the diagnosis of cancer is to be made by the history of the case and the symptoms of dysphagia, pain, cachexia and emaciation. When every patient mentioning the slightest abnormal sensation in the cervical, retrosternal or epigastric region is considered probably not neurotic, but possibly cancerous, surgery will show better results." Palliative treatment should be started early, since it is easier to retain than to regain lost weight and vitality, according to the author. The diet is of utmost importance, a liberal varied menu should be served but all food must be put through a sieve (mesh 25 to the inch), to prevent any lodging in the esophagus. Milk and curd producing foods should not be fed at the same time. **Dilatation** is more safely done by the esophagoscopic approach. **Intubation** may give

good results in some instances, according to Jackson. This writer recommends early **gastrostomy** before the patient's general condition becomes depleted. Deep **x-ray** therapy has given the best palliative results in the author's experience. Here, too, treatment should be given early before cachexia has become marked. Implantation of **radons** is frequently used by the author with arrest of the growth in many instances.

The *surgical aspects* of cancer of the esophagus are discussed by Graham and Ballou (*Ibid* 895). The chief difficulties in this field are inaccessibility of the part and lack of early diagnosis. Surgical approach varies with the portion of the esophagus involved. Figures of location incidence quoted from the literature give the following sites: upper third, 12 to 27 per cent, bifurcation of the trachea, 30 to 48.8 per cent, and lower third, 26 to 63 per cent. The most accessible portion is the cervical, secondly, the abdominal portion. However, the literature contains only a few instances of successful radical operations. In the authors' series of 107 cases, 95 were males and 12 females. The greatest incidence was in the seventh decade, comprising 50 per cent of the series. These authorities believe that gastrostomy should not be done early because of the effect on the morale of the patient. They favor repeated efforts to keep the esophagus patulous before resorting to gastrostomy.

**PEPTIC ULCER.**—In discussing peptic ulcer of the esophagus, a rather rare but interesting lesion, J. Friedenwald, M. Feldman and W. F. Zinn (Trans. Am. Gastro-Enterol. A. 31: 93, 1929) refer to the classification of ulcerations of the esophagus according to Tilleston, who believes that all the following lesions must be excluded be-

fore a diagnosis of peptic ulcer can be made.

(1) Carcinomatous. (2) Due to action of corrosives (3) Due to foreign bodies (4) Occurring in the course of acute infectious diseases (5) Decubitus (6) Due to aneurism (7) Catarrhal (8) Due to traction diverticule (9) Tuberculous (10) Syphilitic. (11) Varicose (12) Due to thrush

Friedenwald and his coworkers state that the first case of esophageal peptic ulcer was described by Albers in 1839, although the first cases studied histologically were presented in 1879. Since that time, 91 cases have been reported in the literature. The ulcers usually occur in the lower third of the esophagus and may extend into the stomach. Although usually single, multiple ulcers have been reported, varying in size from very small to 8 to 10 cm. The most frequent location is the right posterolateral wall, according to the authors. Resembling peptic ulcer of the stomach, the edges are clean cut and punched out in appearance. Perforations have been described. Healing is usually associated with the production of cicatrices. The etiology is similar to that of peptic ulcer of the stomach, but the exact nature is unknown. Vomiting and acid regurgitation are believed to be important, as otherwise gastric juice would not reach the esophagus. In this connection stenosis of the pylorus with associated insufficiency of the cardia has been found in many cases. Of the 13 cases reported by the authors the greatest incidence was in the fifth decade.

In most instances the disease runs an entirely latent course, presenting mild if any symptoms, according to these writers. *Symptoms*, if present, consist of pain which may be epigastric or substernal, radiating to the back, always

worse on swallowing but possibly present between meals. Dysphagia was present in nearly all the cases in this series, vomiting occurred in 54 per cent, and hemorrhage in 23 per cent. Perforation did not occur in any of the 13 cases. The *diagnosis* frequently is not made until perforation or other accident occurs. A history of dysphagia and substernal pain is suggestive, especially if there is evidence of gastric or duodenal ulceration. X-ray study is extremely valuable, and the authors emphasize that it should always precede esophagoscopy. They classify 4 types of defects: (1) mucosal erosions, (2) niche or penetrating ulcer; (3) spastic defects, or (4) perforating. Esophagoscopy yields information regarding the lesion which cannot be obtained in any other way, the authors state. Biopsy is necessary in doubtful cases. Strictures are rather rare in ulcer as compared to the cicatrix from caustics. Differentiation must be made from traumatic ulcerations, ruptured varicosities, lues and malignancy. The course may be short or prolonged, and may lead to cure with or without stricture, or to perforation.

G. B. Eusterman, H. J. Moersch and J. D. Camp (M. Clin. North America 14: 565 (Nov.) 1930) report 3 cases of ulcerations involving the esophagus. The experience of these writers varies from that previously quoted as to the nature of esophageal ulcerations which are often classed as "peptic." They state that "our experience has been confined to single or multiple, large or small, superficial erosions which are often incident to cardiospasm, or which may be the result of trauma. The morphology of these ulcers has no resemblance to chronic peptic ulcer, and they are not discernible roentgenologically."

**Treatment.**—According to Friedenwald, Feldman and Zinn (*loc cit*), treatment is largely dietetic following the usual plan of frequent, small bland feedings as in gastric or duodenal ulcers. **Alkalis** and **antispasmodics** are also indicated. Direct applications via esophagoscope have been recommended. **Duodenal tube feedings** have been used by some. **Gastrostomy**, according to the authors, should be done if healing does not take place following a strict medical plan with the other suggested aids. In the 13 cases reported, relief was obtained in 8 by simple medical management. Local application of **silver nitrate** cleared up 3 additional cases.

### ETHYLENE ANESTHESIA.

See ANESTHESIA.

### EXOPHTHALMIC GOITER.

See THYROID GLAND; GRAVES'S DISEASE.

**EXOPHTHALMOS, PULSATING.—TREATMENT.**—Two cases of pulsating exophthalmos are described by G. L. King, Jr (*Am J Ophth* 14: 786 (Aug.) 1931) in detail, one treated by ligation of the internal carotid followed by hemiplegia and death; the other, untreated, resulted in a temporary recovery. He gives the results of 63 other cases which were reported by physicians in reply to a questionnaire.

Pulsating exophthalmos is a grave, comparatively rare condition, characterized by proptosis of one or both eyeballs, loss of mobility, especially outward, marked chemosis, either a visible or palpable pulsation over the eyeball, and a loud swishing bruit which is synchronous with the radial pulse and is heard upon auscultation. Retinal hemorrhage, cloudiness of vitreous, optic atrophy with loss of vision, thrombosis

of the cavernous sinus, and other intracranial complications are sequelæ.

The causes of pulsating exophthalmos are (1) arteriovenous aneurism between the internal carotid artery and cavernous sinus, (2) aneurism of the ophthalmic artery; (3) vascular tumors of the orbit or surrounding structures, but in most cases it is due to (4) traumatic rupture of the internal carotid in its passage through the cavernous sinus.

Many cases give a history of arteriosclerosis or fracture of the skull.

King suggests the following treatment: 1. **Rest in bed with compression of the carotid artery** on the affected side over a period of time sufficient to make the patient free from cerebral symptoms during the compression period.

2. The use of **gelatin injections** (Locke) during this period of preparation.

3. **Ligation of the common or internal carotid** by one of the various methods suggested for slow compression.

4. If the above fails, **ligation of the orbital veins** before resorting to ligation of the opposite carotid.

G. M. Dorrance (*Ibid* 13:675 (Aug.) 1930), in discussing the operative treatment of pulsating exophthalmos, advises the following as the most satisfactory procedure: A week or 2 after ligation of the common carotid, ligation of all the branches of the external carotid except the internal maxillary and the superficial temporal. Dorrance believes ligation of the veins of the orbit is too dangerous and he is, therefore, opposed to this procedure.

### EYELIDS.—DERMATITIS.—

**Etiology.**—In 3 cases reported by A. W. McAlester, Jr. and A. W. McAles-



ter, 3d (Am J Ophth 14 925 (Sept) 1931), conjunctivitis and dermatitis resulted from wearing white gold spectacle frames. In the first case mild inflammation of the caruncle with an irritation of the brow developed. In the second, a man highly sensitive to nickel, presented a dermatitis over the lids, ears, and nose, and a conjunctivitis. In the third case, a man only slightly sensitive to nickel required 48 hours to develop an erythema from a nickel coin strapped to the forearm.

**"JAW-WINKING."**—A case of congenital unilateral synergy of mastication and elevation of the right upper eyelid in a normal child aged 8 was observed by M. Marin Amat (Siglo méd 86:57 (July 19) 1930). Whenever the child opened his mouth or moved his lower jaw to the left the eye opened. Amat also refers to a case he previously reported in which the inverse phenomenon existed, *i.e.*, the eye was constantly open and closed only when the mouth was opened.

**TUMORS.**—M. Appelmans (Rev. belge sc méd 2 829 (Dec) 1930) treated 75 cases of *epithelioma* of the eyelid with radium. Both the functional and esthetic results were good. He prefers radium treatment for conditions in which there is a choice between radium and surgery.

**VACCINATION, ACCIDENTAL.**—G. F. Munns (Am J Ophth 14 1037 (Oct) 1931) reports a case of accidental vaccination of the eyelids in which a severe vesicular blepharitis, ulceration of both eyelids with loss of lashes but no impairment of vision occurred. He points out that the cornea is especially susceptible to vaccinia, and serious consequences, even loss of the eye, may follow its involvement. He cautions that smallpox vaccine

should be handled with great care and that fresh vaccinations should be protected for 24 hours, or at least until thoroughly dry. For treatment 2 per cent hot boric acid solution irrigations every 4 hours, and instillation of 1 per cent yellow oxide of mercury ointment twice daily, with continuous hot, wet boric acid compresses are used until the acute inflammation subsides.

Munns suggests the use of immune serum. M. Sexe (Bull et mém Soc. de fianc. d'Ophth p 262, 1929) recommends *arsphenamin*. Rollet (Ann. d'Ocul, 1901) reported 45 cases treated successfully by instillations of a 1:500 solution of methylene blue.

**XERODERMA PIGMENTOSUM.**—F. B. Blackmar (Am J Ophth. 14 884 (Sept.) 1931) reports a case of xeroderma pigmentosum, a fatal skin disease which begins in infancy. It appears as warty growths on pigment spots, usually at the mucocutaneous junctures, *i.e.*, the lid margins, the end of the nose and the mouth, and on the exposed parts of the body. The lids may be destroyed leaving the cornea unprotected. Ulcerative keratitis develops, followed by blindness. After 6 to 10 years, malnutrition and death follow.

**EYES.—BINOCULAR VISION.**—A. Duane (Arch Ophth 5 734 (May) 1931) states that the shape, the relative or absolute size, and the position of objects with regard to one another, either in a transverse or antero-posterior plane, are determined by visual projection, the erectness and the location of objects to one side or straight ahead are determined by postural projection. Visual and postural projection combined determine how far away objects are located from the eye.

**EPILEPSY.**—T H Shastid (Am J Ophth, 14 652 (July) 1931) reports a case which he diagnosed as ocular epilepsy. It occurred in a man of 45 who, since the age of 10, had been subject 2 or 3 times a year to numbness in his fingers followed by blurring of vision and accompanied by diplopia which was relieved by closing either eye. After 15 minutes the sight usually returned and headache followed. The general health of the patient is good.

**FOREIGN BODY.—Diagnosis**—From a study of 21 cases of magnetic foreign body in the eye in which the nature of the condition was not diagnosed by the first specialist, L Mills and E C Jeancon (Arch Ophth 4. 194 (Aug) 1930) conclude that failure to recognize foreign bodies in the eye is more common than is generally supposed. They state that failure to use the x-ray in the examination of an injured eye, found later to have contained a foreign body, constitutes negligence.

Sweet's method of localization is considered by C N Spratt (Am. J. Ophth 13 1079 (Dec) 1930) to be the most satisfactory. If the first x-ray is negative, it does not necessarily exclude a foreign body. X-rays from various angles should be taken to avoid obscuration of the foreign body by bone.

**Treatment.**—H L. Begle (J. Michigan M. Soc. 29:345 (May) 1930) believes that the larger the *steel fragment*, the greater is the damage done in perforating injuries of the eye. He finds that small foreign bodies perforating the cornea at the limbus pass through without injury to the lens. He advises **early removal** of a fragment of steel which has lodged in the lens, in order to prevent complete opacification and loss of vision.

The posterior route is preferred by

J H Fisher (Lancet 1 787 (Apr. 12) 1930) for the removal of foreign bodies located behind the lens. In his method scleral sutures are introduced before incising the tissue preparatory to extraction of a foreign body.

Paul G Moore (Am J Ophth 14 750 (Aug) 1931) reports a case in which a small nonmagnetic foreign body, a *copper wire*, was grasped with Kalt capsule forceps through a scleral opening and removed from the vitreous by direct observation through the pupil. An excellent visual result was obtained.

Two cases are reported by E. M. Blake (Am J Ophth 14 1000 (Oct) 1931) in which fragments of *copper wire* which had penetrated the eyeball remained in it for long periods, migrated forward and came through the iris and limbus to the subconjunctival space from which they were removed. All metals produce an inflammatory reaction in the eye, the severity of which depends approximately upon the solubility of the foreign body in the eye fluids. Leber attributes the loosening of the foreign body to a chemical action. Both Wickerkiewicz and Gesang found a connective tissue strand extending from the point of penetration to the foreign body. They believe the leukocytic ferment softens the scar tissue and that increased pressure aids expulsion of the foreign body.

**FUNDUS.—Examination.**—An apparatus for examination of the fundus of the eye with red-free light is described by M. Nakajima (Keijo J. Med 1 437 (Dec 20) 1930). He considers this method essential for accurate diagnosis of fundus disease. Certain changes which are the most important clinical signs of retinal and optic nerve disease, *e g*, changes in the macula lutea, the nerve fiber markings, and the super-

ficial retinal reflections can be much more advantageously studied by the use of red-free light

**Disciform Degeneration of the Macula.**—*Diagnosis*—A case is reported by F H Verhoeff (New England Ophth Soc (Jan 20) 1931, Am J Ophth 14 1050 (Oct) 1931) in which he made the tentative diagnosis of disciform degeneration of the macula. The patient is being kept under close observation, however, so that if the condition proves to be sarcoma of the choroid, early enucleation can be performed. The retina was elevated in the macular region, apparently by a small mass beneath it, but because of the presence of exudates at the periphery similar to those found in retinitis circinata, Verhoeff feels that this is a case of disciform degeneration of the macula.

**INJURIES.**—L Cornil, Hennequin, and P. Kissel (Paris méd 2 135 (Aug 9) 1930) report a case of violent traumatism of the temporomastoid region in a child, age 3, who within a month developed total paralysis of the second, third, fourth, fifth, sixth, seventh, and eighth cranial nerves evidenced by unilateral blindness, "doll's eye," facial paralysis, corneal anesthesia, and neuro-paralytic keratitis. The patient died of suppurative meningitis. At autopsy a hematoma in the right sphenotemporal region and a depressed fracture of the basilar apophysis of the occipital bone were revealed.

According to A. Vogt (Schweiz. med. Wchnschr. 60 1121 (Nov. 29) 1930), temporary or permanent injuries may follow exposure of the eyes to sunlight or artificial light. Injury of the macula lutea occurs by burning of the pigment epithelium and the neuroepithelium by *infra-red* rays, resulting in temporary or permanent scotoma. *Infra-red* rays

are also responsible for glassblowers' cataract. *Ultraviolet rays* of sunlight may injure the cornea and conjunctiva, giving rise to snow blindness. *X-rays* and *radium* are also dangerous, especially to the lens.

J Strebel (Schweiz med Wchnschr. 60 391 (Apr 26) 1930) finds that most eye injuries occurring in skiing are caused by the ski sticks which frequently crush and lacerate the muscle tendons of the eye and also produce more serious injuries.

H L Hilgartner and H L Hilgartner, Jr (Am J Ophth 14.886 (Sept) 1931) report a deep orbital injury by a stick of wood which sectioned the optic nerve.

#### INTRAOCULAR PRESSURE.—

After anesthetizing the eyes of 10 individuals with 2 per cent butyn, L. L. Mayer (Am J Ophth. 14:1015 (Oct.) 1931) instilled various concentrations of epinephrin solution. Tonometric measurements were taken at short intervals after instillation of 3 minims epinephrin in dilutions of 1:1000, 1:500, 1:250 and 1:100. All dilutions produced a fall in tension of 2 to 3 mm of mercury during the second to fifth minute with a return to the previous level by the tenth minute. A direct relationship was found to exist between the decrease in tension and the concentration of epinephrin.

**Etiology.**—W. S. Duke-Elder and P M Duke-Elder (Brit J Ophth. 13: 385 (Aug) 1929) experimented with "perfused eyes" in an isolated animal's head in which the carotid arteries were connected with a perfusing apparatus so as to aerate the blood and stimulate the heart. They conclude that (a) a decrease in concentration of crystalloids or colloids and also apparently a slight alkalosis of the blood produce an in-

creased intraocular pressure, (b) an increase in concentration of crystalloids or colloids and also apparently a slight acidosis produce a decreased intraocular pressure

**MACULAR STAR.—*Etiology.***—F. P. Calhoun (Am J Ophth. 14 95 (Feb) 1931) points out that macular star seen ophthalmoscopically is most commonly caused by increased intracranial pressure and is observed frequently in conditions other than nephritis. He describes 6 cases in which macular star was due respectively to neuroretinitis associated with toxemia of pregnancy, neuroretinitis associated with hyperpituitarism, papilledema as caused by syphilis of the hypophysis; neuroretinal edema in suspected thrombosis and endocrine imbalance, papilledema in suspected cerebellar tumor; and to commotio retinæ with macular hemorrhage. The formation of a macular star is not necessarily a direct consequence of a general disease, but of a local edema caused by various conditions which may be local, as in trauma; remotely local, as in brain tumor, and general, as in nephritis or chlorosis

**MUSCULAR PARALYSIS.—*Etiology.***—Harvey J. Howard (Am. J. Ophth. 14:736 (Aug.) 1931) reports a case of *divergence paralysis* in a woman of 71 who was hospitalized for a carcinoma of the right breast. X-rays showed metastatic tumor of the cranium. The patient complained of sudden onset of diplopia only for distant objects. No paralysis or overaction of any external ocular muscles was found. The patient maintained binocular single vision on a small receding light from the near point out to 1 meter. A diagnosis of divergence paralysis caused by a metastatic growth in the divergence center of the brain was made.

In the literature E. Selinger (Arch Ophth. 4 32 (July) 1930) found 28 cases of *cyclic* or *rhythmic oculomotor paralysis* and reports an additional case which he attributed to congenital syphilis. He found the condition more frequent in females and usually unilateral. The pupil was involved in all the cases reported, the levator palpebrarum in 21, and the ciliary muscle in 11. The spastic features continue during sleep. No definite cause of the condition is known.

**OCULAR DISEASES DURING CHILDHOOD.**—K. Safar (Wien k Wchnschr 43 1232 (Oct 2) 1930), in a discussion of eye diseases which occur during childhood, emphasizes the importance of early recognition of cataract which occurs in rickets, tetany and diabetes, and of glaucoma which is usually accompanied by an enlargement of the eyeball. Early operation in both conditions is indicated. He discusses suppurative conjunctivitis of the newborn, dacryocystitis, acute and membranous conjunctivitis, paralysis of accommodation, blepharitis, suppuration of the lacrimal sac, eczemas and interstitial keratitis. He mentions glioma of the retina, retinitis pigmentosa, and the appearance of the fundus in amaurotic family idiocy. Anophthalmos, microphthalmos, coloboma of the iris and choroid, ectopia lentis, with tremulous iris are listed as some of the malformations found.

**SYMPTOMATOLOGY OF EYE DISEASE.**—Harry S. Gradle (Am J. Ophth. 14:140 (Feb.) 1931) in a statistical analysis finds that one-fourth of all eye patients complain of disturbance of vision; a second fourth complain of asthenopia which may or may not arise from the eye; a third fourth have symptoms referable to some disease of the conjunctiva; and a final fourth have

miscellaneous complaints. The most frequent complaint is headache but less than half of the eye cases presented an ocular cause. One-seventh of the refraction cases were emmetropic, mixed astigmatism, myopia, and hyperopia in the proportion of 1:4:10 were found in the remaining six-sevenths. Two of every 3 patients exhibited some pathological condition.

#### SURGERY OF EYEBALL.—

Coutela (Bull. et mém. Soc. d. chir. de Paris 22:232 (Mar. 21) 1930) reports that for 20 years he has performed without the slightest complications amputation of the anterior segment of the eye as a substitute for enucleation. He resects the eyeball by placing his incision so that it lies in front of the scleral insertion of the recti muscles, in order to preserve motility, and behind the ciliary body, to guard against pain, irritation or incarceration of the ciliary body in the stump. During the operation a supporting needle is held in place to facilitate delimitation and resection of the corneoscleral border and to prevent collapse of the globe. To avoid irritation and infection he does not include the choroid in his suture. The conjunctiva is closed anteriorly in the usual way.

**THERAPEUTICS.**—P. Figdor (Brit. J. Ophth. 14:405 (Aug.) 1930) recommends **diathermy** for the relief of *pain in the eye* from any cause and reports good results in *glaucoma*, *chronic* and *gonorrheal conjunctivitis*, *episcleritis* and *chronic blepharitis*. A few applications usually yield results but the treatment may be continued for more than a year without injury.

W. C. Wilkinson (Brit. M. J. 1:1090 (June 14) 1930) is of the opinion that certain inflammatory conditions in the eye, which do not respond to the ordinary methods of treatment, react to

diagnostic and therapeutic doses of **tuberculin**. He reports 9 cases to support his view.

Four interesting experiences are recounted by D. I. Macht (Am. J. Ophth. 14:726 (Aug.) 1931) in each of which a prescription properly prepared from chemicals conforming to required standards, as proved by subsequent tests, produced unexpected results in the eyes of the patient. A solution of *pilocarpine* 2 per cent with *eserine* ½ per cent. produced mydriasis. A solution of *homatropine hydrobromide* producing extreme and prolonged mydriasis was found to be contaminated with atropine. Pharmacologic tests were necessary in this connection, being much more delicate than any chemical test. A *pilocarpine* solution of high purity was found irritating to the eyes of a patient because of unusual sensitization to small differences in hydrogen-ion concentration.

#### TUBERCULOSIS.—Treatment.—

Almost all fundus lesions of tuberculous origin are found in the choroid, according to R. I. Lloyd (Am. J. Ophth. 13:753 (Sept.) 1930), but occasionally they are limited to a retinal vessel. Vitreous, iris and lens changes usually follow. Uveitis is common in tuberculosis of the eye and indicates an active process. Lloyd has obtained excellent results in this condition by the use of x-rays, employing a silver screen to exclude the rays which burn. *Disseminated choroiditis* is also a tuberculous condition in those cases in which syphilis can be excluded. Lloyd prefers **quinine** to tuberculin for treatment of *phlyctenules*. He believes that this condition is external evidence of a tuberculous process and that *sclerosing keratitis* is a rare type of tuberculosis of the eye.

J. Urbanek (Brit. J. Actinotherapy 5:169 (Nov.) 1930) applied x-rays to

eyes diseased by tuberculosis and found that 3 of 20 cases of *iridocyclitis* showed improvement. These 3 patients had iridocyclitis in both eyes but only 1 eye of each patient was irradiated. The irradiated eye showed a more rapid improvement in each case. X-ray treatment of *keratitis* and *choroiditis* of recent onset also effected improvement.

L. N. Gay (Arch. Ophth. 3:259 (Mar.) 1930) recommends subcutaneous injections of **tuberculin** (bouillon filtrate) for the treatment of ocular tuberculosis. He begins with 0.000001 mg., giving injections weekly for a period of 3 months. A reduction of subsequent dosage is indicated if a focal reaction occurs. He selected 30 cases, which were unsuccessfully treated by other ophthalmologists, and by the use of tuberculin arrested the disease and improved the vision. He suggests that

healing is due possibly to immunological desensitization of diseased tissue. When removal of foci of infection does not result in improvement, tuberculin should be employed.

**TUMORS.—Treatment.**—For the treatment of malignant tumors of the eye and orbit F. H. Rodenbaugh (Radiology, 14:309 (Mar.) 1930) prefers radium to x-rays because of its greater accuracy in dosage and its ease of application. Angiomas, lymphomas, sarcomas, granulomas, fibromas, and nevi usually respond to radiation. For basal cell epitheliomas of adnexa, radiation is better than other methods and clinical cures are obtained. For tumors of the conjunctiva and cornea careful radiation should be done, always bearing in mind the importance of conservation of normal tissue, endeavoring to obtain a clinical regression without loss of function.

## F

**FEEBLEMINDEDNESS IN CHILDREN (HYDROCEPHALUS, MONGOLISM).—ETIOLOGY.**—Recent investigations of feeble-mindedness in children have indicated several especially important etiologic factors. M. W. Barr and E. A. Whitney (New England J. Med. 203:872 (Oct. 30) 1930) classified 3 primary causes of mental deficiency as (1) accidents or injury occurring at birth; (2) acute illnesses or severe injuries in infancy or early childhood, and (3) heredity. The acute illnesses included encephalitis, scarlet fever, gastrointestinal disease, typhoid, infantile paralysis, pertussis, diphtheria, chorea and influenza. In a study of 5000 patients, the authors designated 6 per cent. as belonging to the first group, 28 per cent.

to the second, and 25 per cent. to the third. Five per cent. gave a history of a severe blow on the head in early life. With this classification of the etiology in mind the investigators were convinced that preventive medicine could well be applied in reducing the incidence of mental deficiency. The methods of prevention included (1) sterilization of the present feeble-minded class. In 71 instances of this series the patients themselves had requested such an operation. In questioning 100 parents on this subject, the writers discovered 75 who were in favor of such a procedure, 7 disapproved and 18 gave no answer. (2) A second preventive method suggested was a more rigid marital law which would prohibit the marriage of persons who are physically and mentally unfit. (3)



The other suggestions were better obstetrical care to diminish the number of injuries at birth, and (4) further measures for the prevention of the acute diseases of early childhood

A thorough statistical study of the relationship between the *physical defects* and the mental deficiency was made on 14,176 retarded school children by N A Dayton (M J. and Rec 132 222 (Sept 3) 1930) He concluded that the physical defects were more frequently found in the children with lower intelligence In another study of a series of 43,975 retarded children, Dayton (New England J Med 203 398 (Aug. 28) 1930) investigated the effect of abnormal labor on intelligence In this group, abnormal labor did not occur more frequently in the mothers of the retarded children than in the mothers of the population at large Difficulties of childbirth were more common, however, in mothers whose children had intelligence quotients below 29 or above 90 and there seemed to be a definite increase in the number of abnormal labors of mothers of emotionally unstable children.

The problem of the cause of feeble-mindedness has also been attacked from the standpoint of pathology N W Winkelman (Am J. Psychiat 10:611 (Jan) 1931) regards *cerebral trauma* as one cause of mental deficiency Free blood has been found in 8 to 13 per cent of the newly-born infants, according to recent statistics This condition may lead to meningeal irritation with thickening and adhesions; the cortical irritation, to a proliferation of the superficial glial cells and an interference with the cortical blood supply, which may result in degeneration of the nerve cells Certain infants do not develop a proper pacchionian system nor do they have a

proper subarachnoid space The author believes that hemorrhage into the brain may set up an irritation which produces such lesions Such pathologic conditions were observed in the brains of adults subsequent to definite cerebral trauma Encephalography demonstrated 2 types of lesions, *ie*, (1) those gross in nature causing scar tissue and usually a unilateral dilatation of a ventricle, and (2) other lesions consisting of areas of atrophy and shrinkage, usually in the frontal and parietal areas Encephalography of infants revealed similar changes as a result of birth trauma and subarachnoid hemorrhage The atrophy was thought to be caused by the pressure of overlying localized fluid, a local hydrocephalus due to impaired drainage or by pacchionian body destruction Dehydration and repeated spinal fluid drainage soon after the occurrence of the trauma is the treatment indicated.

A Peiper (Jahrb f Kinderh. 131: 129 (Apr.) 1931) likewise believes that *brain injury* is responsible for much of the feeble-mindedness of infancy, the irritation produced by the injured portions causing motor and respiratory disturbances The resulting convulsions augment the respiratory center irritability, so that irregularities of respiration constitute a frequent symptom of intracranial injury.

In a study of 78 mentally defective patients by means of encephalograms, H Winkler (Arch f. Psychiat 91:495, 1930) could demonstrate pathologic changes in all of those who had had a definite history of *cranial birth injury* Neither the neurologic findings from physical examination nor the degree of feeble-mindedness were related in any definite way to the lesions revealed by x-rays However, in 31 patients the encephalography demonstrated ventricu-

lar abnormalities of some type which could be considered pathologic

The subject of the relationship between *physical stigmata of degeneration and mental deficiency* has arisen again this year with the work of N. H. M. Burke (Proc Roy Soc Med (Sect. Psychiat) 24 11 (Feb) 1931). He studied 3000 feeble-minded patients, all less than 16 years of age, with regard to the abnormalities of their physical development, including spina bifida, meningocele, cleft palate and harelip; deformities of the ears and eyes such as coloboma, cataract, blindness; and face defects (hypertelorism, asymmetry, etc.); defects of teeth and jaws, supernumerary nipples; congenital heart lesions; hermaphroditism; anomalies of the hands and feet, such as extra fingers and syndactylism. Among 1067 patients classed as idiots, stigmata were present in 7 per cent; of 1397 imbeciles, 84 per cent. had stigmata; among 12 feeble-minded, none had such stigmata. Of the *idiot* group, those children classified as Mongols had the highest percentage of physical abnormalities. In regard to the frequency of the occurrence of these defects, those of the eye, including cataracts, blindness, optic atrophy, coloboma were present in 66 instances. Malformations of the hands and feet, such as webbing and extra fingers were most numerous (57 instances); other lesions which were frequently observed were those of the face, such as asymmetry, hypertelorism, etc. (52); asymmetry and deformities of the ear (48); while congenital heart, cleft palate and harelip were less common. The author realized that he had no available "control" group of children with normal intelligence to compare in regard to such physical anomalies and quotes instances of normal mental development in cer-

tain individuals with spina bifida, cleft palate. He is led to believe, however, that there is some slight evidence to indicate that mental retardation may be a question of arrested development with a resulting inadequate cerebral tissue and that there may be similar associated arrests of development in other parts of the body as the hands, feet, eyes, ears, face or elsewhere.

C. S. Woodall (Am J Psychiat 9: 1065 (May) 1930) found congenital syphilis in 7 per cent of feeble-minded patients. Conversely, mental retardation was evident in 20 per cent of patients with congenital syphilis. He, therefore, concluded that syphilis had some influence on the incidence of feeble-mindedness, although in such a series of patients other familial influences were difficult to exclude.

The etiologic significance of *environment and heredity* in producing mentally retarded children must always be borne in mind. A. Myerson (Bull. Massachusetts Dept. Ment. Dis. 14: 108 (Apr) 1930) is inclined to minimize the influence of heredity on feeble-mindedness. He calls attention to the fact that the majority of retarded patients come from homes of the poorest sort, where training has been inadequate; while many of the types of feeble-mindedness, the syphilitic, the cretins, the mongols, the hydrocephalics and microcephalics do not occur in accordance with Mendelian laws of heredity. There only remains a small group of the so-called idiopathic mental defectives who may be influenced by hereditary factors.

G. Ohmstede (Monatschr f Kinderh. 49: 96 (Feb.) 1931) made observations on the *age of parents* of feeble-minded children. Her conclusions from the statistics available indicated that the birth of a feeble-minded child occurred

more often (1) at the end of a series of pregnancies occurring in rapid succession, and (2) in mothers over 30 years of age

**TREATMENT.**—The question of the care and treatment of the feeble-minded child receives greater attention each year. There is agreement in the opinion that such a child should be removed from the ordinary school and given special training. A certain proportion of them usually develop sufficient mechanical skill and self-assurance to be self-supporting during their adult life. J. C. Miller and A. Pelletier (Canad M. A. J. 22 512 (Apr.) 1930) believe that the higher imbecile class with a mental age of 5 to 7 years and the feeble-minded class with a mental age of 7 to 12 years deserve such special training to the extent of their capacities. From the study of the children in their institution, these investigators have been convinced that physical factors are the chief cause of feeble-mindedness. Previous diseases such as meningitis, tuberculosis, trauma and infectious diseases, especially typhoid, scarlet fever and diphtheria are common predisposing agents. *Hereditary factors* most commonly affecting the condition of mental deficiency in children are *alcoholism, tuberculosis, syphilis* and *consanguinity*.

T. Ferguson (Edinburgh M. J. 36 526 (Sept.) 1929) likewise believes that **special schooling** for the mental defective is the best type of treatment, provided that the teachers are specially trained and the children so selected that only the group which can derive some benefit from the special instruction will attend. From an average school district in which there were 12,000 school pupils, 308 retarded children were referred by teachers to the author for special study. All but 12 of this group

were found to have an intelligence quotient below normal. In 70 of this group of 308 pupils such *physical defects* as impaired vision or hearing, tuberculosis, etc., may have had some bearing on their mental condition.

Other investigators have been less optimistic of the result of special training of mental defectives. R. G. Gordon and R. S. Thomas (Brit M. J. 1:1123 (June 21) 1930) followed the progress of such a group of feeble-minded children through the course of several years. Only 37 of a group of 86 could be discharged from the school as ready to take care of themselves in the outer world. Of a total of 52 children who had been discharged from the institution, only 42 per cent had jobs a few years later and were apparently sufficiently well adjusted to their surroundings to be able to maintain themselves without help.

Several definite pathologic conditions are responsible for a small percentage of the total number of feeble-minded persons. Such diseases are hydrocephalus, Mongolism, cretinism, microcephalus, etc. Only the first 2 mentioned will be considered in this section.

**HYDROCEPHALUS.—TREATMENT.**—Various methods of treatment of hydrocephalus have been advanced during the last year. C. Francioni (Scritti medici dedicati a Carlo Comba, ediz. Riv. di clin. pediat. p. 1, 1929, Am J Dis Child 41:458 (Feb.) 1931) treated 2 children with signs and symptoms of hydrocephalus by x-ray with improvement of the clinical symptoms. The rays were directed over the parietal, frontal and occipital areas. The author believes the rays act on the blood-vessels of the brain to cause constriction, and thereby reduce the secretion from the choroid plexus.

The results of restricting the secretion of cerebrospinal fluid by limitation of diet were reported by T. Fay and S. Goldberg (Am J Dis Child 41:730 (Mar) 1931). They restricted the fluid intake of a child of 10 months of age to 12 ounces daily, giving solid and concentrated liquid food. Clinical mental improvement and a reduction of the size of the head resulted. Over a period of 2 months the child did not lose weight or suffer serious disturbance on the diet.

F. Frisch (Wien klin Wchnschr 43:615 (May 15) 1930) reported a method of injecting air into the spinal canal to relieve hydrocephalus. In 38 patients with such a condition the results from this treatment were not uniform, probably because the pathologic lesions varied. To insure any benefit repeated air injections often had to be given. The amount of air injected was equivalent to the number of cc of fluid withdrawn.

C. P. Symonds (Brain 54:55 (Apr) 1931) suggests the term "*otitic hydrocephalus*," in place of the all-inclusive term "*serous meningitis*," for a condition of temporary hydrocephalus which occasionally follows severe ear infections in children and young adults. Although the author does not attempt to explain the mechanism, it is probably inflammatory in nature and accompanies simple otitis media or one of its complications, *i e*, mastoiditis, lateral sinus thrombosis, extradural abscess or meningitis. The symptoms produced are typical of hydrocephalus with the spinal fluid under increased pressure but clear and free of excess cells. The usual methods of treatment, including lumbar drainage, are effective.

**MONGOLIAN IDIOCY.**—It has been suggested frequently that Mon-

golism is the result of some endocrine disturbance and treatment of this condition with glandular extracts has been employed in spite of lack of definite proof of the etiology of the disease. W. D. O'Leary (Am J Dis Child 41:544 (Mar) 1931) made dextrose tolerance tests on a group of 18 Mongolian idiots. Four of the group had had no previous treatment and the administration of 175 Gm (27 grains) of dextrose per kilogram ( $2\frac{1}{5}$  pounds) of body weight caused only a slight elevation of the blood sugar throughout the succeeding 3 hours, a curve rather typical of hypopituitarism. A group of 14 such patients who had had previous treatment with thyroid, whole pituitary gland, or the anterior pituitary portion, had a lowered tolerance for dextrose. That is, after administration of dextrose, the blood sugar rose higher than in a normal person and by the end of 3 hours had not dropped to normal. This suggested that the glandular therapy had been effective in influencing the dextrose tolerance. The author draws no conclusions from his study but comments that more than one endocrine gland appears to be involved in Mongolism.

M. B. Gordon (Endocrinology 14:1 (Jan-Feb) 1930) had an opportunity to make a postmortem examination of the glands of internal secretion of 2 Mongoloid patients aged 14 months and 6 weeks, respectively. The thyroid glands of both were cirrhotic and appeared not to have been functioning. There were no marked changes in the other glands except a beginning involvement of the anterior lobe of the pituitary in 1 instance.

This subject has been approached from a clinical and x-ray view by W. Timme (Bull. Massachusetts Dept.

Ment Dis 14:229 (Apr) 1930; Am. J Dis Child 41:966 (Apr) 1931) X-rays of skulls of Mongolian idiots compared with a normal group showed a higher percentage of enlargement of portions of the sella turcica, and a deeper space beneath the clinoids which connected with the pituitary fossa. Administration of **pituitary extract** together with **thyroid extract** apparently brought about an improvement in growth of the skull, bridge of the nose and the position of the eyes.

### FLAVINE.—THERAPEUTICS.

—The use of an emulsion of flavine in paraffin for **perineal dressings** is reported by M A D Crawford (Brit M J 1 822 (May 3) 1930). He uses small strips of sterile gauze saturated in 1 1000 flavine and paraffin and applies them directly to the perineal scar and vaginal scar after his colporrhaphies. These are applied 24 hours postoperative, after natural sealing of the wound has occurred from serum collection. These dressings are changed following each micturition of the patient. Crawford believes that the wounds heal much more rapidly and with a lower percentage of infections than with other dressings.

W J Sheehan (Brit M J. 1.822 (May 3) 1930) describes 2 cases of **moist gangrene** in which dressings soaked in 1 1000 flavine were applied. He states that this treatment was very satisfactory.

### FRACTURES.—TREATMENT.

—After a number of careful experiments bearing on the relation of blood serum to the *healing* of fractures, Kellogg Speed (J. Bone and Joint Surg 13:58 (Jan) 1931) concludes that dietetic methods or the administration of

calcium salts appears not to affect the rate of flow of calcium away from or into the bones and that in the light of these experiments and observations an estimation of blood serum calcium and phosphorus is valueless from a prognostic standpoint. He considers that attempts to change the blood serum content of these 2 elements are valueless as a sure means of attaining union after a fracture.

### FRACTURE OF FEMUR.—

In the opinion of B A S Bankart (Brit M J 1 8 (Jan 4) 1930), non-union of fractures has but one common cause, and that is insufficient hemorrhage between and around the fractured surfaces. He advises, therefore, **injection of whole blood** in fractures that are notably nonunion ones, and cites as an illustration an intracapsular fracture of the *neck of the femur*. Reduction of the fracture was accomplished with skeletal traction-weights, pulleys, and sand bags. Excellent bony union resulted.

In reporting on the results of treatment in 116 cases, E W H. Groves (J Bone and Joint Surg 12.1 (Jan) 1930) records death in 15 per cent, union in 47 per cent and nonunion in 23 per cent. He does not include extracapsular fractures in this classification. He advises **Whitman maneuvers** in early fractures, but advises **pegging operation of Albee** if there is still non-union in 3 months.

H J Lund (Arch Surg 23.889 (Dec) 1931) reports that after having used, in the past, practically all recognized methods of treatment in cases of fracture of the femur, he has obtained the best results with the **Russell traction apparatus** as used in the method described by R. H. Russell (Brit. J. Surg 11 491 (Jan) 1924). He re-

ports 21 cases treated successfully with this method, which restores the normal tone of the muscle by placing the limb in a natural and comfortable position with a relatively small amount of traction. When the muscles are extended to their normal length, the fragments of the bone tend to fall more or less into their natural alignment, if no soft tissues separate the fractured ends.

Shortening in fractures of the femur is due to tonic contraction of the long thigh muscles, which have their origin from the bones of the pelvic girdle and are inserted into the tibia and fibula. These muscles must be stretched by traction to their normal length in correct alignment, in order to permit the bone fragments to take a normal position. The traction should be applied to the tibia and fibula where the muscles are inserted—never above the knee.

The adductor muscles of the thigh tend to keep the fragments of the femur backward and inward, in the position they have usually been forced into by the fracturing blow, which is usually applied anteriorly or laterally. This adductor muscle action can usually be overcome by varying the degree of adduction or abduction of the thigh by lateral shifting of the position of the head to foot bar, from which is suspended the pulley for the knee-sling rope. The bar is attached overhead to the Balkan frame.

The Russell apparatus, the position of the limb and the mode of extension are the same for fractures of the upper, middle or lower third of the femur. A comfortable position of the limb with the proper amount of traction, will cause the visible displacement of fragments, caused by muscular contraction, to disappear. The position of the proximal fragment can be entirely disregarded.

Traction is removed when there is evidence of firm union and the patient is allowed free motion, in or on the bed, for 1 week. Pain is felt at the points of fracture if union is not firm, and angulation will be noted, in which case, traction should be replaced.

The patient is allowed about, on crutches, 1 week after traction is removed, provided angulation and pain at the points of fracture are absent. If the callus is slight and poorly calcified, a walking caliper splint is worn for accessory support until there is solid union.

Physical therapy, consisting of diathermy, galvanism and faradism, massage and joint motion, is utilized after removal of traction.

**FRACTURE OF HUMERUS.**—The Hope plaster traction method of treating fractures of the humerus, is described by Lawson Thornton (*J Bone and Joint Surg.* 12:911 (Oct) 1930). The skeletal or skin traction may be utilized depending upon the location of the fracture. Patients are ambulatory during the correction. The apparatus consists of plaster-of-Paris arm spica with ratchet windlass attached to the arm portion of the cast, plus either adhesive tape plaster or Steimer's pin skeletal traction. Fractures of the humerus treated with this method do not usually require anesthesia. Local anesthesia or brief gas anesthesia, however, is used for introducing Steimer's pin.

**FRACTURE OF SCAPULA.**—R. T. Findlay (*Ann. Surg.* 93:1001 (May) 1931) concludes from a study of 23 cases of fractured scapulæ that fractures of the scapulæ usually follow great violence. They are usually associated with other injuries, which often interfere with any definite treatment of



the scapula. Most cases are treated by closed method, open operations are unnecessary.

**FRACTURE OF SKULL.**—It has come to be pretty generally recognized that craniocerebral injury often results in pathological conditions which do not support the clinical symptoms and are only observed at necropsy. E. S. Gurdjian and N. H. Schlafer (Arch Neurol and Psychiat 26 583 (Sept) 1931) report 7 cases of head injury in which the orbital surfaces of the frontal lobes were lacerated. The authors conclude that this is a common occurrence and that in the majority of cases such injuries are fatal. The symptoms usually noted are stupor, epileptic phenomena, paralysis and bloody spinal fluid.

J. Kasanin (J Nerv and Ment Dis 69 385 (Apr) 1929) writes on the personality changes in children following cerebral trauma and presents 15 cases. He found that 10 per cent of the cases of the Judge Baker Foundation diagnosed as psychopathic personalities had in childhood or adolescence sustained fractures of the skull or severe cerebral concussion. Of his 15 cases, 13 were regarded as psychopathic and he concludes that severe cerebral injury interferes with proper formations of inhibitory influences. These cases need treatment, mainly psychotherapy, over a long period of time, in correctional institutions and offer a better prognosis than the postencephalitic behavior disorders.

The basis for personality changes probably lies in the multiple military hemorrhages in concussion cases. These are pretty generalized and show no relationship in particular to the point of trauma. A series of fatal cases of cranial traumatism studied at autopsy are reported by H. S. Martland and C.

C. Beling (Arch Neurol and Psychiat 22 1001 (Nov) 1929) with the following conclusions:

Injuries of the head with slight or no evidence of other external injuries are followed in a certain percentage of cases by death or by clinical symptoms indicating structural damage to the deeper parts of the brain. The damage to the brain consists of minute, multiple, punctate hemorrhages, distributed chiefly in the areas supplied by the terminal branches of the central ganglionic system of vessels.

Martland and Beling (*Ibid*) believe that multiple concussion hemorrhages may explain many of the sequelæ of cranial injuries. The clinical picture, varying with the location and extent of the lesions, may resemble that of paralysis agitans, of disseminated sclerosis, of progressive lenticular degeneration, or of chronic epidemic encephalitis.

These writers consider that every case of injury to the head should be considered serious and the patient should receive careful neurologic examination and observation, since an apparently trivial injury may be followed by grave results and may be of great importance to civil and workmen's compensation courts in the estimation of disabilities and the assessment of damages.

The authors quote Morgagni's description of the concussion mechanism as follows: "The brain, driven against the skull and repelled by it, is thus subjected within a moment to 2 motions in opposite directions, if the skull is not fractured the whole force of the percussion is directed against the brain itself." They also quote Bauchet, who concluded that in concussion a more or less extended surface of the brain is affected and that the changes consist only of a vascular injection or of small military

extravasations without notable alteration of the brain substance

**FRACTURE OF SPINE.**—From a careful analysis of 48 cases of compressed fractures of the spine, S W Boorstein (Am J Surg 12 43 (Apr) 1931) concludes that every case of injury to the spine should be examined with extreme care to rule out fracture. Immediate rest should be instituted until the examinations are complete. If it does not endanger the patient, an x-ray should be made immediately, 2 views being taken, *i e*, anteroposterior and lateral, otherwise a delay of 24 to 48 hours may be deemed advisable. If doubt remains, a stereoscope film should be taken as well. If the x-ray is negative but symptoms point to a fracture, another x-ray should be made in a few days, as it may then show the lesion. Diagnosis rests on the history, localized pain and stiffness of the spine.

Fracture of the lamina, transverse and spinous processes, articular processes, the ribs, the bones of the extremities, especially the os calcis, are frequently present, which complicate and influence the treatment.

**TREATMENT.**—Rest on a Bradford frame, is advised by Boorstein (*Ibid*), then plaster jacket or plaster-of-Paris shell. The conservative treatment is attended by excellent results. Full functional return may be expected after 4 to 6 months of recumbency and hyperextension with the spine immobilized in a shell or jacket.

**Early operation** is indicated where the x-rays show a dislocation of the bone pressing on the spinal canal.

Patients with fresh fractures should rarely be subjected to operative interferences. In cases of complete trans-

verse lesions of the cord, open interferences can do no good.

In cases of incomplete lesions where there are indications for operation it is more beneficial to wait 2 or 3 weeks.

Later nerve operations are indicated in cases of progressive symptoms and where adhesions are present.

All patients having injury in cauda equina should be operated on, since the nerves of the cauda equina are capable of regeneration.

In late cases where pain still exists, Nature has not ankylosed the injured region of the spine and if the patient is to return to strenuous back-bending labor, an ankylosing operation should be considered, which is likely to save time and allow the patient to labor without apprehension.

**UNUNITED FRACTURES.**—An ununited fracture in which there is little or no displacement or angulation of fragments may be treated satisfactorily, according to D. B. Phemister (Surg Gynec and Obst 52:376 (Feb.—No 2 A) 1931), by the simple application of whole thickness splint grafts or in some cases of osteoperiosteal grafts, to the fragment surface bridging the fracture line and held in place by the sutured soft parts. Intramedullary grafts are unsuited for cases of nonunion, but the sliding graft may be used in fresh fractures and in delayed union. This author points out, however, that when marked displacement of fragments is the indication for operation, a broad inlaid graft which is turned on edge and made to fill both medullary cavity and slot cut in cortex affords a suitable method of treatment of some cases of nonunion of large bones.

## G

**GALL-BLADDER.** See BILIARY TRACT.

**GASTROINTESTINAL TRACT.—PHYSIOLOGY.**—The problems of present-day gastroenterology have been discussed by W. C. Alvarez (*Am J. M. Sc* 182:441 (Oct) 1931). Regarding gastrointestinal physiology, he believes that the greatest advances will come in the study of motility. It now appears probable that peristaltic waves tend to travel aborally largely because the upper part of the bowel is more active, more irritable, and more responsive to every stimulus than is the lower part. Since the tonus and activity of the intestinal wall decrease gradually from the duodenum to colon, it can be said that food follows a gradient of force similar to the one which causes oil to flow along a pipe line. It now seems probable that a reversal of the gradient of forces in the bowel can be produced by any agency that will depress the functions of sensitiveness and activity more in the upper part, or which will stimulate them in the lower part more than in the upper.

As to nervous control of the intestine, Alvarez is convinced that both the vagus and the splanchnic nerves serve largely as brakes to the bowel. Without these brakes, he states, the gut tends to respond to every stimulus, and the animals often die of diarrhea and inanition. The writer believes that the symptoms of indigestion are largely produced by disturbances in the motor functions, and that secretory disturbances play a relatively minor rôle, although exact knowledge in this field is still wanting.

In discussing functional disturbances of digestion, Alvarez points out the rela-

tion between emotions and gastrointestinal physiology. It has been shown that mental distraction, fright, worry, disgust, or annoyance at meal time can for hours afterwards interfere with the emptying of the stomach. It is also known that these mental disturbances can either greatly delay or else markedly stimulate the movements of the bowel. The exact mechanics of these disturbances is as yet unknown. Constipation, coarse diet and constitutional make-up are other factors having an important relation to functional disorders of the gastrointestinal tract.

Certain digestive symptoms, Alvarez believes, are due to early organic disease which is difficult or impossible to diagnose by present methods. Mild degrees of gastritis or enteritis, hepatitis, early cirrhosis, slight pancreatitis, infection with neurotropic viruses, mesenteric lymphadenitis, and disturbances of circulation are mentioned as being possible etiologic factors in many questionable cases.

Other subjects demanding more investigation include the etiology of peptic ulcer, and the cause and relief of abdominal pain.

**GERMAN MEASLES.** See RUBELLA.

**GLAUCOMA.—ETIOLOGY.**—Glaucoma is not more common among the Jews than among other people, according to Aaron Brav (*Am J. Ophth.* 14:48 (Jan) 1931). He attributes his own case of glaucoma to the wearing of low minus cylinders in the early stages of presbyopia, in association with disturbances of general metabolism. He recovered completely without surgery or the continued use of miotics.

**PATHOLOGY.**—In discussing the pathology of chronic simple glaucoma, R. Castroviejo (Arch Ophth. 5:189 (Feb.) 1931) states that in this condition the whole organism presents a generalized angiosclerosis and that all the intraocular vessels present atheromatous degeneration. He believes that glaucoma depends upon a nervous—endocrine—humoral circle, with a decrease in nutritional exchanges in the vitreous and lens, producing a state of turgescence which pushes the iris forward and narrows the anterior chamber. The metabolic or nutritional exchanges are due to an alteration of the osmotic equilibrium between the blood-pressure and the intraocular fluids.

Castroviejo points out that by the combined action of the engorged vitreous and lens, contraction of the ciliary body which pushes the lens forward, the thickened aqueous humor, and the generalized sclerosis of the tissues, the periphery of the iris is pressed against the spaces of Fontana and glaucoma is produced.

From a clinical and pathological study J. S. Friedenwald (Arch Ophth. 3:560 (May) 1930) concludes that edema of the ciliary body and hemorrhagic, serous, and fibrinous extravasations in the ciliary processes are always present in acute glaucoma. He believes that edema must arise from changes in the capillaries, because the larger vessels were found to be free from disease.

J. S. Friedenwald and H. F. Pierce (*Ibid.* 3:574 (May) 1930) made an experimental study on the mechanism of acute glaucoma with animal eyes by injecting histamine which acts on the capillary walls and increases the permeability of the endothelium. Edema of the ciliary body with fibrinous and serous extravasations followed, accom-

panied by a rise in tension, mydriasis, and shallowing of the anterior chamber.

W. H. Wilder (Am J Ophth. 13:681 (Aug.) 1930) believes that in mild serous iritis or cyclitis, increased tension is produced by the secretion of aqueous which has a greater viscosity than the normal aqueous.

**TREATMENT.—Nonoperative.**—W. Alexander (Klin Monatsbl f Augenh. 84:65 (Jan.) 1930) reports 2 cases in which alcohol injection of the Gasserian ganglion gave permanent relief from pain in absolute glaucoma and ciliary neuralgia. He considers this the only method for permanent relief, without cosmetic deformity, in uncontrollable pain in a blind and particularly in a functioning eye.

J. Krasso (Ztschr. f. Augenh. 68:163 (June) 1929) investigated the possibility of influencing glaucoma by x-ray irradiation of the thyroid and concluded that it is possible to find cases of *chronic glaucoma* in which there is a connection between hyperfunction of the thyroid and vasomotor disturbances on the one hand and glaucoma on the other. It is not yet possible to determine just what cases of glaucoma will respond to this treatment. He finds that basal metabolism is not a determining factor.

Wilder (*loc. cit.*) prefers homatropine as a mydriatic because its effect can be counteracted, and pilocarpine as a myotic because it is less irritating than eserine. He also suggests the use of levoglucosan in *glaucoma*. He finds that a La Grange or an iris-inclusion operation gives better results than trephining.

**Operative Treatment.**—Although glaucoma, in the vast majority of instances, has been controlled by miotics for 35 years, E. de Grósz (Arch. Ophth. 5:327 (Mar.) 1931) is of the opinion

that **operation** is practically always required and is still the best treatment

**Iridencleisis** is recommended by O R Wolfe (Am. J Ophth. 14:769 (Aug) 1931) for the relief of glaucoma arising in eyes after cataract extraction. He states that secondary glaucoma following cataract extraction is rather common, and loss of vision is often attributable to this complication. He prefers the iris hook to the forceps and uses the water-tight suture to prevent prolonged hypotony.

Good results were obtained in 35 of 40 cases of primary and secondary glaucoma in which **iridotaxis** was performed by G H Bell (Arch. Ophth 3:194 (Feb) 1930). By elimination of septic foci, the exclusion of syphilis and other diseases, and the prescribing of a diet of lactose and acidophilus, more than 50 of his glaucoma patients have not so far come to operation owing to reduction in ocular tension which followed this treatment.

Bell recommends the **Reese iridectomy** in *acute inflammatory glaucoma* and **iridotaxis** in the *chronic type* of glaucoma, in *secondary glaucoma* following anterior uveitis, and in that following cataract extraction.

George F. Suker (Am J Ophth 14:732 (Aug) 1931) states that while no other operation is as satisfactory as **iridectomy** for *acute glaucoma*—not secondary, or primary glaucoma—an iridectomy is to be deprecated in all cases of chronic glaucoma and in simple glaucoma or when there are no inflammatory symptoms. He believes that the only logical anatomical drainage within the eye is suprachoroidal, not subconjunctival, and for this purpose recommends **Mauksch's operation** (suprachoroidal iridotaxis or intraocular iridencleisis), which is a combination of

nearly all the filtration operations. He describes the Mauksch operation technic as follows. The conjunctiva is dissected to within  $2\frac{1}{2}$  to 3 mm. of the limbus as for cyclodialysis or trephine, a scleral section 4 to 5 mm long is then made at about 6 to 7 mm. from the limbus, parallel with the cornea, and through the sclera down to the choroid. A liberal cyclodialysis is made with a cyclodialysis spatula, the pupillary edge of the iris is grasped with iris forceps and gently drawn into this channel almost to the scleral section but not beyond it, in order to avoid leaving the iris subconjunctivally. The iris is massaged to adhere at the inner edge of the scleral wound. Almost a complete turn is made with forceps while withdrawing the iris, giving the latter a spiral turn, so that the pigment surfaces will face each other, thus insuring a drain. The conjunctiva is closed with 2 or 3 sutures and atropine is instilled. By this method, Suker effected a reduction in the tension of all the *subacute* or *chronic* types of *glaucoma*.

A. S. Green, L. D. Green and M. I. Green (Arch Ophth 3:297 (Mar) 1930) find that **trephining** has the following advantages over other operations for glaucoma; (1) It is most successful; (2) it is easier to perform, and (3) it leaves the eye without disfigurement. They recommend 2 important steps in the operation, *i e.*, (1) placing the trephine so that it leans toward the scleral, not the corneal, side, and (2) performing iridotomy or iridectomy the moment the iris prolapses into the trephine opening, without permitting the prolapse to increase, and without taking hold of the iris with forceps.

The technic of the **trephining** operation for glaucoma is reviewed by R. H. Elliott (Am J. Ophth 14:999 (Oct.)

1931) and he explains the rationale of each step. He emphasizes the following points in his technic. (a) The wide angled conjunctival flap of maximum thickness, (b) splitting of the cornea and not cutting it with a sharp instrument, (c) a 2 mm trephine opening half in the cornea and half in the sclera, (d) a small iridectomy leaving the trephine opening free from the iris and a continuous suture for closing the conjunctival wound. He offers many practical suggestions in handling difficult cases of glaucoma.

Five cases of *chronic simple glaucoma* are reported by William Zentmayer (Am J. Ophth. 14:617 (July) 1931) in which satisfactory results were obtained by **sclerocorneal trephining**. He has found that sclerocorneal trephining has afforded a fairly high percentage of cases in which tension was permanently reduced with improvement in central and peripheral vision. In a considerable percentage, however, the visual function of the eye was damaged by frank iritis, an insidious iritis with pigment proliferation and deposit of fibrin, subcapsular opacities, and finally, loss of the eye from late infection which resulted in 2 cases. Because of the sequelæ, Zentmayer resorts to this operation less frequently than formerly.

**GLYCOSURIA.**—The subject of glycosuria is a most interesting one because it seems generally conceded that the majority of cases are those of diabetes mellitus, but when it is considered that this is only one of several types of glycosuria, the picture is somewhat changed.

To understand the various types and forms of glycosuria all forms must first be divided into 2 classes: (1) those glycosurias not associated with an in-

crease in the concentration of the blood sugar, and (2) those cases associated with an increase in the concentration of sugar in the blood.

Under the first classification will fall *renal diabetes*, which type may be simulated experimentally by the introduction of phlorizin, which causes a liberation of glucose through the kidneys without any effect upon the concentration of the blood sugar. The intravenous injection of solutions of sodium chloride will also cause such a glycosuria, as well as the administration of caffeine, theobromine and diuretin. These latter examples are only transient and are of very little significance clinically.

Under the first classification it is simplest to describe first that form of glycosuria which develops following the ingestion of large quantities of carbohydrate. This type is frequently spoken of as "*alimentary glycosuria*." Another type is seen experimentally following a puncture of the floor of the fourth ventricle. Clinically this type may be seen following the cerebral injuries. Many substances injected into the blood in proper concentration will bring about a glycosuria. These are the chlorides, iodide, bromide and nitrate of sodium, lithium, potassium or strontium. A lack of oxygen will also result in a glycosuria. This type is seen in carbon monoxide poisoning, cuare, strychnine and tetanus intoxication. Various anesthetics are capable of inducing a glycosuria, *i e*, chloroform, ether, morphine and chloral. A newer form of glycosuria has been recently described experimentally and known as the *hepatic form*. In this type the introduction of ether into the portal vein results in a glycosuria. Lastly, and most common of all forms of glycosuria associated with an increase in the concentration of the



blood sugar, is true diabetes mellitus which may be classed as a pancreatic insufficiency

The work of C J Munch-Petersen (Brain 54 72 (Apr) 1931) is of interest in that he describes a case of glycosuria of *cerebral origin* which supplies a valuable supplement to the theory that sometimes in these conditions there is a connection between the function of the kidney tubules and the neurohypophyseal apparatus. Even though his investigations of cerebrally continued glycosuria do not form a foundation for a definite etiologic or pathogenic division of these conditions, a threshold test which he describes and filtrating mechanisms have made it possible to group these diseases more definitely when working clinically with glycosurias. By comparing this grouping with other clinical features, as the course of the disease, and with the pathologic anatomic investigations, it may perhaps be possible to determine more accurately their etiologic and pathogenic factors.

P B Landabure (Semana méd 2 1358 (Oct 30) 1930) reports the case of a patient, aged 5 years, who since the age of 5 months had shown a permanent glycosuria not modified by diet or insulin. The author states that in cases of infantile diabetes, acidosis appears unexpectedly even if constant attention is given to the patient, while in his patient the presence of glycosuria was well tolerated, though the patient never received special care for diabetes because he has not shown himself to be a true diabetic patient. The glycosuria in this instance was associated with a normal glycemia. There was a diminution of the renal threshold. Of over 2000 cases which the author has observed this is the first one who had a renal glycosuria of nondiabetic origin.

Three cases of *renal glycosuria* are reported by F N Allan and F H Vanzant (Am J M Sc 180 670 (Nov) 1930) in which each showed a clear response in the excretion of sugar when complicated by a surgical operation or infection. In fact, the excretion of glucose may be so great as to result in the development of ketosis, unless sufficient care is taken to prevent it. In this respect the condition simulates diabetes mellitus, but the mechanism involved is entirely different. In the former there is apparently an increased permeability of the kidneys and in the latter, increase in the defect of the utilization of dextrose appears to be the important factor.

**GOITER.** See THYROID GLAND

**GOLD COMPOUNDS.—UN-TOWARD EFFECTS.**—J R Driver and J N Weller (Arch. Dermat. and Syph 23·87 (Jan) 1931) report on the use of gold compounds in the treatment of lupus erythematosus and other tuberculous conditions of the body. In one of their cases where rather heavy doses were given on 2 occasions, death resulted and at autopsy the liver showed a picture resembling that seen in acute yellow atrophy. Death had been preceded by fever, prostration, generalized erythema, loss of hearing, icterus and hemorrhages from the vagina. In this case, death was thought to be due to an idiosyncrasy on the part of the patient to gold. These authors stress quite strongly the need of using gold compounds less indiscriminately than in the past and feel that the therapeutic effectiveness of small doses is equal and the incidence of reaction is greatly less than when larger doses are given.

L. Nové-Josserand, J. Gate, J. Charpy, Josserand and P. Cuilleret

(Bull Soc franç de dermat et syph 38. 117 (Jan ) 1931) report a series of 3 cases with gold pigmentation of the skin in children who had been receiving gold compounds as therapy in pulmonary tuberculosis. In all cases the pigmentation resembled that seen with silver compounds and was noticeable only in those areas which were exposed to sunlight.

H Schlossberger and W Menk (J Chemotherapy 8 41 (July) 1931) relate at length their experiments with gold compounds on *spirochetal* and *trypanosomic* diseases. They finally concluded that with certain gold compounds destruction of the organisms is possible. However, a practical difficulty arises since doses which might cause destruction of the spirochetes may in the weakened condition of the patients produce toxicity. When given later, after the spirochetes have penetrated the central nervous system, the gold preparations, like arsphenamine, do not always produce sterilization. If, however, a mixture of neoarsphenamine and a gold compound called "*solganal*" is administered, the total annihilation of the spirochetes, including those in the central nervous system, may be obtained.

## GRAAFIAN FOLLICLE AND CORPUS LUTEUM. — CYSTS. —

Massive hemorrhage of a follicular cyst or of a cyst of the corpus luteum may present a picture identical with ectopic pregnancy. The moderate hemorrhages, if right-sided, are often mistaken for acute appendicitis. H P Miller (J A. M. A 96 1569 (May 9) 1931) reports 4 cases.

The etiology of these cysts may be classified as *general*, such as infections and disorders of nutrition, and *local*, such as torsion or thrombosis, oophoritis, trauma and excessive coitus.

The symptomatology depends upon the type of bleeding. Most cases start with a sharp colicky pain suggesting a perforated viscus, but localized to the right or left side of the pelvis. There is tenderness and rigidity, slight fever and leukocytosis. Miller has also observed a frequency of urination. A posterior vaginal puncture will reveal free blood in the peritoneal cavity. All patients should be **operated upon immediately** because there is no way of knowing the extent to which the bleeding may go.

**GRAVES'S DISEASE.** See THYROID GLAND

## H

**HAIR.—RELATION OF ENDOCRINE GLANDS.**—In a study of the relation of the endocrine glands to the growth and distribution of hair, Z K Cooper (Arch Dermat. and Syph 21:1007 (June) 1930) states that dermatology was perhaps one of the first fields to be affected by the development of the new growth of biology and endocrinology which has occurred during the past 30 years.

Bramwell reported as early as 1893 the results obtained in cases of psoriasis, lupus vulgaris and acute eczema by the internal administration of thyroid extract. Since that time, as endocrinological study has advanced, there has been an ever increasing interest in the relationship between the glands of internal secretion and the skin and its appendages. Because the information regarding this relationship to the hair is widely

scattered, a review of some of the more important literature is given

Disturbances in the growth of the hair have been noted in both hyperthyroidism and hypothyroidism

In cases of myxedema resulting from *hypothyroidism* the hair is thin, dry, lusterless and may fall out. This is true of the scalp, the pubic and axillary regions, the eyelashes and eyebrows, as well as the hair of the shins, thighs and forearms.

*Alopecia areata*, present in cases of hypothyroidism, has been successfully treated by Hertoge, by Gordon and by Strandberg under **thyroid** administration. In a case reported by Saunders, in which the left lobe of the thyroid was removed from a child 5 years old, the resulting myxedema with loss of hair was entirely relieved of all symptoms by thyroid treatment

The typical pallid, lifeless appearance of the skin, hair and nails should always suggest disturbed metabolism, in general, and thyroid hypofunction, in particular.

That hereditary *dystrophies of the hair and nails* may indicate hereditary hypothyroidism is supported by cases reported by Barrett. Such deficiencies had occurred in a family for 6 generations, affecting 14 of 61 members. In the case of a patient reported by this author as treated with **thyroid** medication a marked improvement occurred, affecting even the hair and nails.

*Old age changes in the skin* and its appendages may be due to a diminution of thyroid activity. Starr believed that these defects may be obviated or removed by the constant use of **thyroid extract** as age advances. It must be admitted that this is a somewhat unusual suggestion. He supported his views with reports of cases from his practice

*Hyperthyroidism* has been considered by Sabouraud as the cause of some cases of *alopecia areata*. Numerous cutaneous complications are found in *Graves's disease*, among them many cases of *alopecia areata* as reported by Hyde and McEwen in a study of 111 cases of this syndrome

Experimental work on animals has produced conditions similar to those found in the clinic. In the case of rabbits, cretinism produced by the removal of the thyroid gland was followed by loss of hair and a retardation of its regeneration. After feeding suitable amounts of thyroid gland the hair grew normally in these animals.

Thyroid feeding accelerated the growth of hair in some normal animals, while in others no such results were obtained

Albino rats deprived of the thyroid gland showed a retarded growth of hair. When these animals were fed thyroid gland the hair grew normally. In many thyroidectomized lambs, but not in all, the wool became coarse and easily pulled out. Goiter in domestic animals results in the absence of hair or wool in the animal so afflicted

The thyroid gland seems to be definitely related to the pilary system but the relationship is scarcely proved to be a direct one.

*Chronic tetany* produced by removal of the *parathyroid glands* is frequently accompanied by dystrophies of the hair, teeth and nails and pigment anomalies and chronic ulcerations of the skin. Observed cases in man and experimentation upon animals lead to the opinion that the hair and skin are at least secondarily affected in disturbances of the parathyroid glands.

In disturbances of the *hypophysis*, as in disorders of the thyroid, changes in

the pilary system are to be found under conditions both of hyposecretion and hypersecretion

The tendency to *hypertrichosis* is marked in many persons afflicted with *hyperpituitarism*. Women may develop a heavy growth of dark hair between the breasts and on the abdomen and legs, and sometimes also a beard. In 100 reported cases of acromegaly, hypertrichosis occurred in 53, while a decrease of body hair occurred in 7. These were reported by Davidoff, reviewing clinical histories. The hair is thick, wiry and oily. In pituitary disturbances, in general, Rowe and Lawrence found hypertrichosis in 28 per cent of 400 reported cases, and decrease in the body hair in none.

The cutaneous features of primary *hypopituitarism* are the reverse of those of acromegaly. When it originates in adult life, there is a tendency for the hair, even of the head, to become thinned (Cushing). In the majority of the cases, there is a decrease in the amount of hair and, in many males, a feminine distribution. Dwarfism, hypoplasia of the sex organs and deficiencies, or inverse distribution of hair are usually associated with defects in the pars anterior of the hypophysis as demonstrated by autopsy and experimentation.

Removal of the anterior lobe in dogs was followed by the skin becoming dense, dry and less movable. The hair became bristly and tended to fall out in patches. A lessening of the sexual activity and atrophy of the ovary or testicle were also observed.

Animals fed with *tethelin* (the growth-controlling constituent of the anterior lobe) showed exceptionally good coats, abundant and glossy, at an age when normal animals have begun to lose their hair. This lends color to the

supposition that *tethelin* is a specific stimulant of the growth of epithelial tissues. These observations on hair were incidental, but are suggestive of an approach to the study of the influence of the pituitary gland upon hair growth.

The cessation of *thymus* activity at puberty suggests that the thymus gland's internal secretion is concerned with the inhibition of sexual development and its associated hair growth. Cases of *thymicolymphaticus* are recorded with anomalies of the distribution of hair. Emerson considered the scantiness of hair to be a point in diagnosis of this condition. The thymus is said to persist in eunuchs. These have scanty pubic, axillary and facial hair.

Tumor of the *pineal* gland has been described as resulting in a syndrome characterized by abnormal height, abnormal growth of hair, premature development of the genital organs and sex instinct and mental precocity. Kidd ascribed to the pineal gland the function of inhibiting premature genital development and sex characteristics. The pineal secretion is thought to be nullified by the mature genital secretion. In chicks it was demonstrated that removal of the pineal body caused premature development of secondary sexual characteristics. There is little evidence to show that the pineal gland has an effect on the skin.

Certain abnormalities in the distribution and growth of hair are correlated with change in the *suprarenal glands*. Bulloch and Sequeira found that premature development of the beard and pubic hair in children is accompanied by premature ripening of the sex organs and in such cases found suprarenal changes of a hyperplastic and neoplastic nature. They also found some cases in which suprarenal atrophy was associated with

nondevelopment or disappearance of pubic hair and genital hypoplasia. A case with one missing suprarenal gland and sclerosis of the other gland showed *alopecia totalis* and *skin pigmentation*.

If hypertrophy of these glands occurs during fetal life, pseudohermaphroditism may result. Occurring during infancy, such cases show hypertrichosis, hypertrophied clitoris, small uterus and poorly developed ovaries.

Tumors of suprarenal glands occurring before puberty result in hypertrichosis, adiposity and precocious puberty. After puberty the condition causes abnormal development of hair, adiposity, and in females an arrest of menstruation.

There is a tendency in children with hypernephromas, for male primary and secondary sex characters to increase at the expense of the female.

In a series of 18 cases of tumor of the suprarenal glands, 14 occurred in girls and 4 in boys. Overgrowth of pubic hair was found in all cases, overgrowth of hair on the face in 14 cases and in the axilla in 5.

Many cases of suprarenal virilism in women and girls have been reported—moustache, beard and whiskers were developed to a noticeable degree, with body hair distribution characteristic of the male sex.

Little experimental work regarding the suprarenal influence upon hair growth has been done but Castaldi produced increase in weight and unusual length of hair by feeding young guinea-pigs dry extract of suprarenal cortex of beef.

Although definite knowledge of the steps bringing about the results is lacking, yet there is evidence that disturbed functioning of the suprarenal glands results in disturbed growth of hair.

The *sex glands* would seem to exercise an influence upon the growth and distribution of hair in that the absence of *testes* or *ovaries* tends to the occurrence of hair distribution typical of the opposite sex. Whether this influence is exerted secondarily through the effects produced upon other endocrine glands is an unsettled question.

The fact that terminal hair appears in cases of precocious puberty in which there is only a gonadal involvement strengthens the theory of a more or less direct relation between the sex glands and the hair.

Extract prepared from ovary and placenta injected into senile rats improved their general condition, caused the growth of new hair on bald spots and general smooth, glossy appearance of the entire coat.

Transplantation of *testicles* of young sheep into aged animals by Boronoff resulted in more abundant and longer wool than in the controls. So much doubt and confusion surrounds the subject of transplantation of glands that results can be accepted only with caution.

On the side of negative evidence must be taken into account reported cases of pseudo-hermaphroditism in which persons presenting the normal secondary sexual characteristics of the female were found to possess testes and, again, other cases (4 reported by Bell) in which the internal genitalia were female while the secondary characteristics were chiefly masculine. One of these cases shaved regularly, and in 2 the pubic hair had appeared at an early age.

It has been held that the development of secondary masculine characteristics in the female is due to an excessive suprarenal secretion which overcomes that of the ovary. This theory is supported by the fact that in many cases of

suprarenal hypertrophy there occurred atrophic changes in the ovaries

Of *pluriglandular disturbances* the syndrome of Timme is the most clear cut as involving the thymus, the pituitary and suprarenal glands. Among other defects accompanying it is a sparse growth of hair with an invert type of distribution.

Baker described a thyro-testiculo-hypophyseal (suprarenal) syndrome often involving trophic disturbances of the nails and teeth, loss of hair and other disturbances of the secondary sex characters. Such patients come to resemble eunuchoids.

The subject of the *interrelationship* between glands of internal secretion and their relation to hair is extremely complicated. The relationship of the sex glands, the pituitary gland, the suprarenals and the thyroid gland to hair growth may be direct or through interaction between these several glands upon each other. At present it is impossible to definitely say.

**SUMMARY.**—The question of the growth and distribution of hair is as yet but little understood. Hypertrichosis is found in hypopinealism, hyperpituitarism, hypergenitalism and hyperfunction of the cortex of suprarenal gland. However, since few really quantitative studies of even the normal variations in the growth of hair have been made, it is difficult to determine just how great is the influence of the endocrine glands. With endocrine disturbances, there are also striking differences in the growth and distribution of the hair as between men and women. For example, hypopituitarism causes the male to assume the female type of distribution of hair, but it does not cause the female to assume the male type of distribution. Hyperpituitarism, on the other hand,

causes the male to become more male in type and the female to become male in type. Hyperplastic tumor of the cortex of the suprarenal gland also causes the male to become more masculine in type of distribution of hair, and the female to assume the male type of hair distribution.

Several conditions have been made responsible for the female distribution and scantiness of hair in both sexes. Among these are status thymicolymphaticus, infantilism, lymphatism, and eunuchoidism. These are in all probability, however, but primary conditions causing changes in some gland or glands of internal secretion that are, in turn, responsible for the condition of the hair.

It may be said, with Kraus, that "in fact, we know practically nothing of the causes of changes in the hair either as to growth or distribution, and it seems unfortunate that a sign so easy of observation should be so little understood."

#### HEADACHE. — ETIOLOGY. —

The almost universally held opinion that headache is due to stretching of the dura is doubted by F. Tilney (Bull. New York Acad. Med. 6:69 (Feb.) 1930), who advances clinical and experimental evidence that sudden changes in intraventricular pressure and irritation of the meningeal vessels are more often responsible for headache than stretching of the pachymeninges.

The difficulty that is supposed to attend the determination of the disease responsible for a headache is largely a myth in the opinion of Thomas Reilly (Journ. Med. Soc. N. J. 27:528 (June) 1930), who believes that the clinical cause is usually detectable without trouble. He outlines the characteristic pain patterns describing the localized,



boring headache of lues, the frontotemporal site of toxic aches, the suboccipital morning pain experienced in uremia, the dull headache which the cardiac suffers after exercise, the feeling of "head compression" of the arteriosclerotic, and the localized morning tenderness of the sinus cold.

The importance of history in the differential diagnosis of headache is emphasized by G. D. McGregor (Southern Med and Surg 92 68 (Feb) 1930), who tabulates the data essential in the case study, *i.e.*, family history, occupation, home hygiene, habits, constipation, and menstrual history—all requiring special stress. Many authors point out features of the special types of headache

Among the *dental* causes listed by E. C. Kettner (U. S. Vet. Bur. M. Bull. 6 46 (Jan.) 1930) are unerupted teeth, hypercementosis, exposed dentine, jaw cysts, and cavities in the teeth. Headache from these sources is usually neuralgic in site and character.

*Gastric* factors are often forgotten in the opinion of J. J. Walsh (Internat Clin 3 135 (Sept) 1930), who believes that so simple an agency as irregularity in eating habits can provoke repeated headaches

Tilney (*loc. cit.*) describes *migraine* as "sick headache" and suggests that it can readily be diagnosed on the basis of normalness between attacks, recurrence of the paroxysms, and severity of the migranous episodes

H. W. Haight (J. Med. Soc. New Jersey 27. 43 (Jan) 1930) pleads for a retention of the old term *rheumatic headache*, describing patients with swollen lymph glands in the tendon sheaths at the back of the neck who were relieved from headache after a month of physiotherapy.

*Pituitary* headache occurs only in women, in the experience of L. H. Mayers (Endocrinology 14: 319 (Sept.-Oct.) 1930), who recognizes the patient type in whom it occurs as being short, obese, long-legged, intelligent, dysmenorrheic, and energetic.

C. L. Martin (Am J Roentgenol 24: 267 (Sept) 1930) sees no reason for abandoning the traditional term, *menstrual headache*, for frontal or occipital pain accompanied by nausea occurring during the menstrual cycle

The patient with a prominent aquiline and consequently a crowded nasal fossa, is, according to G. R. Halloran (M. J. Australia 2. 779 (Dec. 13) 1930) susceptible to *sinus headache*. Absorption of air in the frontal sinus results in a vacuum which is associated with low grade pain above the eyes, worse on trying to read, and tender at the upper, inner angle of the orbit

Involvement of Sluder's nasal ganglion may produce pain in the lower part of the head and jaws with earache and rhinitis in the experience of Halloran (*loc. cit.*). This is the so-called *nasal ganglion neurosis*. In the diagnosis of sinus headache transillumination is often inadequate. Leo J. Hombach (Laryngoscope 40: 753 (Oct) 1930) suggests lipiodol and x-ray, the arc lamp and nasopharyngoscope as further diagnostic aids in these cases. In maxillary sinus headache, Hombach warns, the pain may be over the eye, due to anastomoses between the supra-orbital and infraorbital nerves.

*Ocular headache* is commonly due to hypermetropia and astigmatism. In I. S. Tassman's opinion (Med. Times New York 58: 229 (Aug) 1930) 90 per cent. of all people have errors of refraction. Therefore, it is not surprising that ocular headache is so widespread.

**TREATMENT.**—Efforts at treating headache rationally rather than symptomatically have marked the recent literature. Less attention is being paid to drug treatment and more to specific forms of therapy. Tilney (*loc cit*) prefers to treat *migraine* between rather than during attacks. The simple formula of outdoor life, rest, and relaxation will often terminate the cycle of paroxysms. During the acute attack he recommends nitrites or oxy-quinoline, the latter in 5 gram (0.3 Gm) doses.

Certain forms of headache are amenable to a surgical approach. E. R. Carpenter (M. J. and Rec. 132:375 (Oct. 15) 1931) lists craniostenosis, brain tumor, localized meningeal lesions, brain abscess, skull injury, and certain spinal fluid disturbances, as causes of headache responsive to surgery.

For the treatment of the pressure sense and headache associated with hypertension, J. R. O'Hare and L. H. Hoyt (New England J. Med. 199:1207 (Dec. 13) 1928) suggest the use of extract of mistletoe in the form of "intra de gui" (*Viscum Album Gui*) as a 2 per cent. solution of the dried extract. It is given in 3 to 5 c.c. (48 to 80 minims) dosage before meals. They report that within 10 days, 75 per cent of their patients were relieved of the headache of high blood-pressure. William Barrow (California and West Med. 33:887 (Dec.) 1930) used this mistletoe preparation and confirmed the reports of Hare and Hoyt, obtaining equally good results.

Physiotherapy in the form of mud packs at 100° F. (37° C.) is recommended by Haight (*loc. cit.*) for rheumatic headache. The pack is given daily for 2 or 3 weeks, 15 minutes exposure each day. Infundibular pitui-

tary extract in 0.5 c.c. (8 minims) doses was effective in L. H. Mayer's series (*loc cit.*) of pituitary cases. The preparation must be given hypodermically, daily for 10 days, then less often. Thyroid and polyglandular preparations are not recommended.

In the cases of menstrual headache cited by Charles Martin (*loc cit.*) artificial menopause (by x-ray) was found effective, but limited to women over the age of 40.

Cocainization of Sluder's ganglion should relieve genuine cases of the nasal ganglion neurosis, according to Halloran (*loc cit.*) For nasal and sinus headaches, Louis Weiss (Laryngoscope 40:892 (Dec.) 1930) has used vaccines with good results. He also recommends intranasal surgery in more obstinate cases.

Treatment of post-traumatic headache by insufflation of air at lumbar puncture seems to be gaining greater acceptance. First suggested by W. Penfield (Surg. Gynec. Obst. 45:747 (Dec.) 1927), the procedure was used with good results by L. F. Barker (Internat. Clinics 1:8 (Mar.) 1929) and subsequently by D. Boyd (Arch. Surg. 18:1626 (Apr.) 1929). H. L. Skinner (Am. J. Surg. 8:842 (Apr.) 1930) reports a case of traumatic headache relieved in this manner.

**HEART DISEASES IN CHILDREN.\*—DIAGNOSIS.**—A method for the determination of the size of the heart in infants has been reported by F. von Bernuth (Monatschr. f. Kinderh. 48:25, 1930). X-rays were taken at a distance of 1.5 meters. He found that if the figure resulting from multiplying the body length by the greatest transverse diameter of the lungs is divided by

\* See also Cardiovascular System

the transverse diameter of the heart, the result is a constant, which varies between 31 and 47 with an average of 39. If it is below 31, the heart is abnormally large, if over 47, the heart is unusually small.

**PROPHYLAXIS.**—The need of organized medical effort in the detection and treatment of the initial stage of heart disease is stressed by W. Coleman (J. A. M. A. 96:1904 (May 30) 1931). He suggests the education of the public by means of such publicity and organized campaigns as have been used against tuberculosis and cancer.

**CONGENITAL DISEASE.**—*Etiology.*—An unusual type of cardiac anomaly together with an unusual family history of cardiac disease has been reported by H. B. Sprague, E. F. Bland and P. D. White (Am. J. Dis. Child. 41:877 (Apr.) 1931). The case described was that of a 7 months' infant in whom the diagnosis of *congenital idiopathic cardiac hypertrophy* was confirmed at necropsy. A sister of this patient was found to have what appeared to be an identical cardiac lesion, a half-sister had a cardiac lesion, which was diagnosed as patent ductus arteriosus, a maternal aunt had rheumatic heart disease, a great aunt, heart disease of undetermined etiology, a sister of the latter had 2 living boys, but her 10 female children died in infancy or childhood, several from disease suggesting a congenital cardiac condition. The authors suggest the probability of an inheritance of a tendency to congenital cardiac anomaly.

M. Steiner and M. Bogin (Am. J. Dis. Child. 39:1255 (June) 1930) have also reported a case of idiopathic cardiac enlargement, with which was associated a state of "thymicolymphaticus". They found 20 other cases of true idio-

pathic hypertrophy in the literature, 4 being associated with status thymicolymphaticus.

Congenital heart disease and reduced fertility, both masculine and feminine, have a common cause, in the opinion of W. D. Reid (Arch. Int. Med. 48:721 (Nov.—pt. 1) 1931).

The importance of congenital malformations of the heart lies, not in their number, for they are uncommon, but in the fact that they may produce invalidism in, and shorten the life of, one so afflicted, and sometimes cause the death of an infant at birth or shortly thereafter.

Because embryologists apply the term monster to fetuses and full term infants having congenital malformations, Reid considers that opinions and studies concerning monsters in general, apply to fetuses and patients with congenital cardiac deformity.

Congenital malformation of the heart is believed to be of accidental or unknown origin by most clinical writers. Reid quotes a variety of different opinions, however. Mall, who claimed that monsters are produced from normal embryos, by influences of their environment, capable of destroying tissue and arresting development, Thompson, who blamed interference with the health of the mother for faulty embryonal development of the heart, and disbelieved in intrauterine endocarditis; Keith, who asserted heredity alone was the cause; Meyer, who suspected a germinal origin of cardiac malformations; and Abbott, who found more congenital heart disease in brothers and sisters than in ancestors of patients so afflicted.

It is noted that malformed fetuses have been produced experimentally by treating the embryo with various chemicals; thus, potassium is said to arrest

cardiac development, and sodium to produce spina bifida. Duplications of certain vertebrate embryos have been produced by (1) ultraviolet and x-rays, (2) mechanical separation and pressure, (3) changes in the salt concentration and oxygen content of the surrounding medium.

Monsters, both spontaneous and experimental, are usually involved principally in only one particular system of the body. This indicates that there is an increased sensitivity of the tissues of the various systems of the body at certain periods of their development, and that the effect of an unfavorable influence upon the development of a fetus depends upon which tissue is most sensitive at the time of the deleterious influence.

Spontaneous abortions are the greatest preventive of birth at term of infants with congenital heart disease, as they terminate the vast majority of all pregnancies in which any form of monstrous change in the fetus has occurred. B. Whitehouse (Editorial J. A. M. A. 94:489 (Feb 15) 1930), has written of 2 cases in which threatened abortion was controlled with difficulty to term, only to result in anencephalia and spina bifida, respectively. Most early abortions present abnormal fetuses, but in abortions occurring late in pregnancy the fetus is usually normal.

A. W. Rowe (J. A. M. A. 95:1219 (Oct 25) 1930) believes that repeated abortions may be due to endocrine abnormality in one or both parents, and that, if the disorder in the parents is corrected, subsequent pregnancies may go on to full term.

Reid is also of the opinion that defective germ plasma in the human male, as a cause of monsters, is unproven, but still a possibility. Imperfect implanta-

tion of the ovum and abnormal development of the chorion and decidua are factors predisposing to embryonal malformation.

When congenital anomalies recur in the same family, the cause may be considered a constant condition, whereas a pregnancy with abnormal fetus followed by a pregnancy which is normal indicates a transitory parental fault.

Birth of an infant with congenital heart malformation, or any monstrous departure from the normal, should occasion an exhaustive study of both parents to detect any abnormality of their endocrine functions or other disease. Proper treatment of any deficiencies or diseases found should be completed prior to future pregnancies.

#### RHEUMATIC CARDITIS.—

**Diagnosis.**—Not all children who are suspected of heart disease have organic lesions. This is emphasized again in the work of M. Seham, M. J. Shapiro and E. H. Hilbert (Am. J. Dis. Child. 42:503 (Sept) 1931), only 46 per cent. of 809 patients passing through their heart clinic having been found to have organic heart disease. Of these, 18 per cent had congenital lesions, 74 per cent were rheumatic in origin; only 3.6 per cent were due to other causes, and 4.4 per cent were undiagnosed. The chief problems of differential diagnosis occurred in children with the following conditions: (1) A systolic murmur, with or without circulatory signs and symptoms, (2) rheumatism and a systolic murmur in which the heart has escaped carditis; (3) rheumatism and a systolic murmur that ultimately develops into chronic endocarditis, and (4) congenital heart disease, especially patentcy.

They found that an adequate history taken by means of a questionnaire best served their purposes in securing ade-

quate data. They stress the importance of using all available data in the making of a diagnosis. (1) etiologic, (2) structural, (3) functional, (4) x-ray and esophographic, and (5) electrocardiographic.

The diagnosis of rheumatic heart disease is essentially a diagnosis of rheumatic infection in any of its protean forms. The heart may be the seat of the initial infection and the only manifestation. Every rheumatic child is a potential heart case. W. Coleman (J. A. M. A. 96:1904 (May 30) 1931) considers that each child with so-called potential heart disease has a damaged heart. The tendency of rheumatic heart disease is to heal, with or without deformity of the valves. This tendency to heal is the crux of the argument for early diagnosis and treatment.

**Prophylaxis.**—*Tonsillectomy*.—The value of tonsillectomy in the prevention of rheumatic disease or its recurrence continues to be a most important question. A. D. Kaiser (J. A. M. A. 95:837 (Sept. 20) 1930) reiterates his previous statement that in his series of cases, first attacks of rheumatic manifestations occur from 30 to 50 per cent less in tonsillectomized than in non-tonsillectomized children, particularly if the tonsillectomy is done early in life, in the 3 to 7 years age group. In contrast to his previous report (J. A. M. A. 89:2239 (Dec. 31) 1927) he now finds that recurrent attacks of rheumatic fever are not affected by tonsillectomy.

The value of tonsillectomy in the prevention of first attacks of rheumatic fever is not attested by all writers.

#### ACUTE ENDOCARDITIS.—

**Prognosis.**—An interesting analysis of the remote prognosis of acute endocarditis in 100 cases is made by J. L. Morse (Am. J. Dis. Child. 42:735 (Oct)

1931). Only patients who were seen during their first attack (10 to 30 years before this article was written) are included in this study. Of these, 36 are dead, 3 are cardiac invalids, and 61 are alive and well. Of the 61 who are considered as well, 37 have normal hearts, 18 have slightly damaged hearts, and the hearts of 6 were not examined. The course was short in most of the fatal cases. 33 per cent died within 4 weeks of the onset, 66 per cent within 4 months, and two-thirds of the remainder died within 5 years. Those cases which were associated with rheumatism did not seem to do so well as those which followed upper respiratory infections. Recurrences were less frequent than is usually considered to be the case, but were more frequent in those with slightly damaged hearts than those with normal hearts. 40 per cent. in the former and 11 per cent. in the latter. Morse finds, however, a hopeful note in this latter figure, as it shows that despite repeated attacks of acute carditis, recovery may take place. Only 1 of his patients who is considered well has a diastolic murmur. The outcome, in his opinion, depends more upon the care received than upon any other factor. The care seemed to be complete bed rest over a long period, with limited activity for still longer periods.

#### BACTERIAL ENDOCARDITIS.

**Diagnosis.**—Acute bacterial endocarditis is uncommon in childhood and rarely seen during infancy. J. M. Sansby and L. M. Larson (Am. J. Dis. Child. 39:1261 (June) 1930) report its occurrence in an infant 5 weeks of age. The onset of the illness was sudden with high temperature, frequent and loose stools and listlessness. The course was stormy and the child died on the sixth day. At no time was heart in-

volvement suspected. Necropsy revealed a bacterial endocarditis.

A very good clinical description of *Streptococcus viridans* endocarditis as it occurs in childhood is given by C. B. Leech (Am J M Sc 180 621 (Nov) 1930). The onset is usually gradual with lassitude and pallor, although it may be more acute. The infection is commonly superimposed upon an old rheumatic carditis or upon a congenital heart defect. The course varies, with an average of several months' duration. Fever is irregular. Petechia and Osler's nodes are common and the spleen frequently palpable and tender. In the latter stage the skin is of a yellowish hue, sometimes described as *café au lait*. Urinary findings vary between normal and those of an acute nephritis. The heart sounds vary with the location of the lesion and the mitral valve is most frequently affected. The heart is usually slightly to moderately enlarged.

**PERICARDIAL EFFUSION.**—**Diagnosis.**—The diagnosis of pericardial effusion may be confused with that of pneumonia, pleural effusion or pulmonary infarction. L. P. Sutton (Am. J. Dis Child 41.467 (Feb) 1931) points out certain features which are characteristic of this condition.

There is no material change in the position of the heart, but the inflamed pericardial sac may be distended much beyond its usual capacity. Distention is somewhat more to the left than to the right side. As the effusion increases in size, the lung is pushed upward and laterally, until the pericardium actually comes in contact with the posterior wall of the chest. The percussion note is dull to flat posteriorly below the angle of the scapula, and breath sounds are apt to be bronchial, with an associated bronchophony due to the compression of

the lung. There may be an area of resonance between the posterior dullness and the left cardiac border.

The x-rays should rule out the presence of fluid in the pleural space. The author recommends posterior puncture for diagnosis and drainage, suggesting that a point at about the center of dullness but more towards the spine than the axilla should be chosen.

**HEART FAILURE.—Treatment.**—Working on the premise that heart failure in children is practically always associated with active inflammation and that while the beneficent effects of digitalis in active cardiac disease are established, this is not generally conceded to be the case during active disease, L. P. Sutton and J. Wyckoff (Am J Dis Child 41.801 (Apr) 1931) have studied the effect of digitalis in children with heart failure. All of their patients showed some improvement in the signs of heart failure when fully digitalized. In most of the cases they were able to attain the effects of digitalization without producing the toxic effects of the drug. The effective dosage of digitalis for children is comparable to that required by adults (0.15 cat units per pound of body weight).

In contrast to the conclusions drawn by Sutton and Wyckoff are those of S. P. Schwartz (Am J Dis Child 39 549 (Mar.) 1930), who reports the results of digitalization in 2 patients with active rheumatic carditis and some evidences of heart failure. His patients received 3 c.c. (48 minims) of the tincture of digitalis daily, 1 receiving 24 c.c. (6 drams) of the drug and the other 32 c.c. (8 drams). Auricular fibrillation developed in each case after the administration of the respective doses of digitalis. The first patient died 7 hours after the establishment of the



fibrillations The fibrillations disappeared in the second patient within 6 days after discontinuing the digitalis Because of these dangers, the author concludes that digitalis therapy is contraindicated in children with rheumatic fever and signs of cardiac insufficiency

**HEMATURIA.—CLASSIFICATION.**—R Rinaldi (Arch ital di urol 6 624 (Oct ) 1930) makes the following classification of renal hematurias (1) hematurias of clearly nephritic origin; (2) non-nephritic but symptomatic hematurias of evident renal causations, *i e*, traumas, calculi, tuberculosis and tumors, (3) symptomatic hematuria pointing to an evident hemorrhagic diathesis; (4) hematurias of renal origin in which a latent blood defect is present or in which minimal nephritic lesions are discoverable, developing in a particular vascular area and cryptogenic hematurias

Two cases of so-called *essential* hematuria are reported by J Miller and O H Young (Canad M A J 24 354 (Mar ) 1931) In both instances pyelitis was present. The close approximation of the large venous channels in the pelvis of the kidney and the presence of hemorrhage and inflammatory infiltration in the perivascular tissues of these veins lead the authors to believe that the bleeding probably has its origin from the veins in the sinus of the kidney Regarding the name of "essential hematuria," they believe that it will eventually be dropped as causes for the bleeding are found It would be exaggerating to state that pyelitis of the calyx-papilla angle should be substituted for it, but the latter term is certainly applicable for a number of the cases. In the meantime, the authors believe that the kidney pelvis should be examined

carefully in all organs removed for serious bleeding not explainable by tumor or other grossly evident pathologic change

**ETIOLOGY.**—The association of hematuria with cholecystopathy is reported by H Edelmann (Med Klin 26 1817 (Dec 5) 1930), who found that this condition of hematuria exists in about 3 per cent of his cases of biliary tract disease He advises a careful examination of this tract to make a correct diagnosis and it should always precede the more serious instrumental urologic examination In many instances he observed that with the cure of the cholecystopathy by removal of the gall-bladder, there was a disappearance of all cellular elements from the urine

C S. Swan (New England J Med 202 901 (May 8) 1930) reports 7 cases of hematuria which present the serious possibilities which may arise from it He urges a most careful microscopic examination of the urine, even though there may be no definite genitourinary pathology, in order that the patient may have the advantage of the proper differential urologic diagnosis if blood is present The author quotes Eisendrath and Herman in stating that two-thirds of all cases of hematuria are caused by lesions of the genitourinary tract, while 70 per cent. of these affect the upper and 30 per cent. the lower tract Swan considers the term of "*essential hematuria*" merely a cloak for ignorance and believes that it should be eliminated The frequency with which exploratory laparotomy and appendectomy have been performed because of an incomplete urinary investigation is borne out by the statistics of the Mayo Clinic, in which approximately 20 per cent. of the patients suffering

with stone in the ureter were subjected to a previous appendectomy without relief

### HEMIANOPSIA.—ETIOLOGY.

—Five cases of homonymous lateral hemianopsia in diabetic patients are reported by G E de Schweinitz (Am J Ophth 14 1053 (Oct) 1931) who also refers to 18 other cases in the literature and points out that this field defect is not due directly to diabetes but to vascular lesions in the occipital lobes

### HEMOGLOBINURIA.—E Licht-

mann (Med Klin. 26 735 (May 16) 1930) reports the case of a man, aged 34 years, who consulted him because of blood in the urine. He stated that whenever he was exposed to dampness or cold, the urine became almost black, the condition being accompanied by chills, painful joints and an oppressive sensation in the chest and fever. In childhood he was subject to hematuria following cold baths. Rosenbach's test of giving the patient a cold foot bath for 10 minutes was followed by blood in the urine. A diagnosis of paroxysmal hemoglobinuria was made and since the author reasoned that because liver therapy is especially effective in the hemolytic forms of pernicious anemia, it might also prove effective in this case. Liver was prescribed and the patient improved rapidly and markedly. He stated that he gained weight and his exposure to cold did not precipitate hematuria. The liver diet was discontinued for 6 months followed by a positive Rosenbach's test, whereupon liver therapy was immediately instituted and within 2 weeks the test was negative.

A Zaffagnini (Arch. ital. di urol 6: 71 (Mar) 1930) reports a case of appendicitis which was complicated by

hemoglobinuria. On the sixth day of a regular postoperative course, the stitches were removed. There was some tenderness and a temperature of 99° F. (37.2° C). In the afternoon the patient had pain and a chill. He turned pale and collapsed but recovered with the use of stimulants. The temperature rose to 102° F. (38.9° C) and the urine was scanty and red colored. No red blood cells were present but by long centrifugation a hemoglobinuria was discovered. A hypodermoclysis of 250 cc (½ pint) of physiological salt solution was given and no food for 24 hours. The following day the patient developed an icterus. The temperature dropped to normal in 10 days. Later, the urine was free of all hemoglobin and the patient was dismissed fully recovered.

### HERNIA.—VARIETIES.—

N Novara (Arch ital di chir 27 483 (Oct) 1930) describes in detail a case of *mediogastric strangulated herma* and, in that connection, gives a survey of *inguinal herma of the stomach*, reporting chronologically the 19 cases described in the literature.

D D Iraeta and E Harguindéguy (Bol Soc de obst y ginec 8 237, 1929) describe a case of double uterus, in which at operation they found a rudimentary uterus, ovary, and tube in the hernial sac, and a uterus and adnexa free in the abdominal cavity. Up to 1923, the author had collected 78 cases of *inguinal herma containing the internal genitalia*.

C P G Wakeley (Surg. Gynec Obst 51 256 (Aug) 1930) states that the majority of *herma containing internal genitalia* occur in patients under 1 year of age. Wakeley states that torsion and strangulation are the most fre-

quent complications. Corroborating this statement, L. Allegri (Policlínico 36 1832 (sez prat) (Dec 16) 1929) has reported a *strangulated tubo-ovarian hernia* in a 6 months' old child.

E. Sciaky (Policlínico (sez prat) 36 1383 (Sept 30) 1929) reports a case of diverticulosis of the bladder with protrusion into the right inguinal canal. The author discusses 3 varieties of *hernia of the bladder*.

V. Jura (Policlínico 36 1833 (sez prat) (Dec 16) 1929) describes a case of *diverticular hernia* in which he operated on the newborn child 12 hours after birth. Meckel's diverticulum was connected with the umbilicus by fibrous bands that represented residua of the omphalomesenteric duct. D. Petit-Dutaillis (Bull et mém Soc nat de Chir de Paris 56 180 (Feb 8) 1930) also successfully operated on an *umbilical hernia* in an infant shortly after birth. In this instance the hernial sac contained liver which was adherent.

J. C. Masson and A. H. McIndoe (Surg Gynec Obst 50:29 (Jan) 1930) report a case of right *paraduodenal hernia* in association with marked obstruction of the herniated small intestine, due to an isolated tumor resembling carcinoma but of hyperplastic tuberculous origin. This is the thirty-third example of right paraduodenal hernia reported, the sixteenth patient with this condition to be operated on, and the fifth to recover following operation. Isolated hyperplastic tuberculosis of the small intestine is rare, only 7 cases have been reported. The 2 lesions in association make the case unique. The presence of tuberculosis in the hernial sac is interpreted as being due to stagnation of food and to the slowing of the intestinal current in the sac. The conditions were thus similar

to those under which the same type of tuberculosis occurs in the cecum.

**ETIOLOGY.**—In the etiology of hernia, *heredity* plays the major role, according to W. Birkenfeld (J. A. M. A 94 1633 (May 17) 1930), not only evidencing itself as inherited hernia, but the *localization* of the hernia and its *variability* are also inherited. Thus, in a family in which inguinal hernia has shown itself, the other members are more apt to exhibit inguinal than umbilical hernia. There is another factor besides the predisposition to hernia which enters in and so makes the hereditary picture somewhat obscure, that is, the strain to which the person is subjected. Hence hernia, especially of the inguinal type, is observed far more frequently in males than in females, due to their greater physical activity, in conjunction with the developmental differences in the inguinal regions in the 2 sexes. Birkenfeld states that if there is a history of heredity in the case of hernia, recurrence of the difficulty after operation is found in 11 per cent. of the cases, whereas if there be no history of hernia in the family, recurrence is noted in but 4 per cent. This striking difference gives a quantitative estimate of the relative rôles of heredity and environment in the production of this defect.

W. K. Connell (Brit. J. Surg. 18:16 (July) 1930) points out, in his experience, that the East African female has apparent immunity to hernia. The author operated upon 208 cases, only 2 having occurred in women—one being an umbilical and the other a femoral hernia.

H. Schutz (Deutsche Ztschr f Chir. 223 367 (Mar) 1930) found 20 cases of *traumatic interstitial abdominal hernia* on record and adds a personal case. The man had been caught between 2

electric carts and squeezed severely, the handle of the steering gear hitting him in the left inguinal region. There was no external wound, but soon afterward it became evident that intestinal loops were palpable under the skin of the abdominal wall. This was confirmed at operation. A hole was found in the external oblique and transverse muscles just above the internal inguinal ring through which the intestine had forced its way out into the tissues of the abdominal wall.

According to C F Thompson and J V Reed (Am J Surg 12 458 (June) 1931), *traumatic hernias* occur as complete and incomplete indirect hernias. Complete indirect inguinal hernia, whether spontaneous or traumatic, is the result of the dilatation of a preexisting funicular process. Incomplete indirect inguinal hernia is either the early stage of the complete type or it is the bulging of the normal peritoneum following a giving way of the fibers of the aponeurosis of the external oblique. In all types of traumatic hernias the sudden stretching of the peritoneum causes immediate disabling pain, often accompanied by nausea. If these symptoms are lacking, the hernia is not the result of a single strain. In hernias with thin-walled sacs it is impossible to determine the age of the hernia by the size of the sac.

I Z G Nel (J M A South Africa 3 710 (Dec 28) 1929) relates the case of a girl, thrown heavily from a horse, landing flat on her abdomen. Ten days after her accident, signs of perforation developed. Operation disclosed a strangulated loop of jejunum, dragging with it a portion of the pancreas through an opening in the transverse mesocolon.

**PATHOLOGY.**—According to V L Schrager and J T Gault (Surg

Gynec Obst 52 836 (Apr) 1931), fibrous peritonitis at the neck of a hernial sac is of common occurrence. The etiology of this *circular fibrous ring* at the neck of the sac is probably an aseptic traumatic peritonitis, the result of repeated muscular contractions at the internal ring. The authors claim that this condition is responsible for a number of cases of strangulation.

**DIAGNOSIS.**—E Traum (Med Klin 27 506 (Apr 2) 1931) points out that the so-called *internal hernias*, that is, those in reformed peritoneal pockets, may lead to diagnostic errors. He then reports the case of a man, aged 64, who suddenly developed severe pains in the hypogastric region on the right side. The pains persisted to the following day and the patient had 3 attacks of vomiting and frequent eructations. Flatus and evacuation of the bowels ceased since the onset of the pain. An acute appendicitis was assumed and an appendectomy was considered advisable. However, the appendix showed no signs of inflammation. The incision was extended and the entire small intestine was examined. Diverticula were not found, but one loop of the small intestine showed signs of a prolonged incarceration. Resection of this loop was not necessary because after the loop had been freed its peristalsis and red coloration returned. The loop had been incarcerated in an opening of the posterior parietal peritoneum closely beside the cecum. In the conclusion the author points out that if laparotomy is done for the purpose of appendectomy and the appendix is found to be free from pathologic changes, the possibility of an internal hernia should be taken into consideration, particularly when symptoms of intestinal occlusion are present. In such cases the intestine should be care-

fully examined so as not to overlook an internal hernia

E M Miller (Surg Clin North America 10 375 (Apr) 1930) reports 2 cases of *strangulated hernia* caused by a perforated appendix. The first case was that of a man 29 years old, who presented signs and symptoms of a strangulated right *inguinal hernia*. At operation, the hernial sac was found to contain edematous omentum which was covered with plastic exudate. A right rectus incision disclosed a ruptured appendix and localized peritonitis. Appendectomy with drainage was followed by recovery.

The second case, also that of an elderly male, showed a mass having the appearance of a right *femoral hernia*. At operation, the mass proved to be the sac of a femoral hernia which was filled with pus. The pus had entered the sac from a large pelvic abscess secondary to rupture of the appendix and general peritonitis.

The differential diagnosis between eventration of the diaphragm and *diaphragmatic hernia* has been drawn from movements of the costal margins, x-ray findings, studies of intragastric pressure, pneumoperitoneum, the findings at operation and the results of faradication of the phrenic nerve. When the nerve on the side of the diaphragmatic hernia is stimulated, a response of the diaphragm is seen under the fluoroscope. In eventration, stimulation of the nerve fails to cause contraction. R H Overholt (Ann. Surg. 91 381 (Mar) 1930) describes a patient showing hernia of the diaphragm in which the x-ray findings and the result of operation were shown. Radical operation for repair of the hernia was simplified by preliminary paralysis of the phrenic nerve and the use of spinal anesthesia.

X-rays of substantial value in diagnosis of *diaphragmatic hernia*. S W Harrington (Surg. Gynec. Obst. 51 504 (Oct) 1930) noted 8 cases in detail and summarizes 30 more upon which he has operated in the past 4 years. The ages of the patients were given as ranging from 7 months to 70 years, 13 being females and 17 males. The symptoms are frequently complex, due to the various factors involved, and depend to a certain extent on interference with the function of the herniated abdominal organs. Gastric hemorrhage is not common and is usually associated with severe gastric incarceration. Use of the x-ray early in the period of presence of symptoms is often sufficient for the diagnosis.

**COMPLICATIONS.**—R Chabrut (Presse méd. 38 1223 (Sept 10) 1930) describes several cases that show what serious results may follow even a slight *contusion* of a hernia. Whether the contusion is followed by a strangulation (complete or incomplete), a generalized peritonitis or a hemorrhage, the only safe rule is to operate as quickly as possible, even when reduction of the hernia takes place spontaneously. **Early operation** is especially important when peritonitis is involved, for instance, in 10 cases observed, only 2 patients survived, on both of whom operation was performed within 2 hours after the contusion.

**RECURRENCE OF HERNIA.**—According to E Moen (Norsk mag. f. Lægevidensk. 91 624, 1930), in the follow-up examinations on patients operated upon for *inguinal* and *femoral hernia* during the period January 1, 1918 to December 31, 1927, it was found that 2.21 per cent of the inguinal herniæ had recurred. The incidence of recurrence of such herniæ as given by

others ranges from 1.5 to 6 per cent. Among the causes of recurrence are complications in the healing process, such as infection and the formation, during the operation, of hematomata which may hinder closure of the hernial opening and provide a favorable medium for the development of infection. Other important causes are insufficient isolation of the hernial sac and insufficient mobilization of the oblique muscles, which result in such great tension when the muscles are sutured to Poupart's ligament that the muscle fibers atrophy and lose their supportive capacity. In some cases the cause is natural weakness of the musculature. Recurrence may be brought about also by vomiting or stubborn constipation after the operation.

In E. Husted's (Biblot f laeger, 123 297 (July) 1931) cases, the recurrences of *femoral hernia* were 20 per cent. In a selected group of such cases, 15 per cent recurrences were noted. There was recurrence of 6.5 per cent after *inguinal* methods.

**MORTALITY.**—In Husted's (*Ibid*) 1688 cases, the postoperative mortality was 1.5 and 2 per cent, mainly with pulmonary complications and emboli in the pulmonary artery.

H. Godard and C. Palios (Rev de chir, Paris 67 476, 1929) reporting on 122 cases of *strangulated* and *gangrenous hernias*, state that recovery occurred in 104 cases, with a mortality of 14.8 per cent. The authors claim that the prognosis depends on the degree of toxemia. Thus, in *strangulated umbilical hernias* with extensive intestinal stasis, the mortality was 36.3 per cent, whereas in *strangulated inguinal* and *femoral hernias*, a mortality of from 2 to 4 per cent was noted.

**TREATMENT.**—According to H. Steuernthal (Med. Klin 26:1598

(Oct 24) 1930), the small *umbilical hernias* in children which do not extend beyond the normal width of the umbilical ring, can usually be cured by suitable **plaster bandages**. By the end of the first year they are usually cured. However, if conservative methods do not have the desired results, **surgical treatment** has to be resorted to. This is especially the case when the hernia is more extensive. For cosmetic reasons, care should always be taken that the umbilicus is preserved.

H. Salzer (Wien klin Wchnschr 42 674 (May 16) 1929) points out that high removal of the sac is sufficient in the **radical treatment** of *inguinal hernia* in children. A plastic operation on the muscle may favor the later development of direct inguinal hernia by causing muscle atrophy. Operation should not be considered before the end of the first year unless the hernia interferes with the child's development or becomes incarcerated. It is usually impossible to obliterate the processus vaginalis completely by a truss, and unless this is done an area favoring hernia remains. Funicular hydrocele should be treated surgically at the same time as the open processus vaginalis. In cases of cryptorchidism, the testicles should be implanted in the scrotum if this can be done without tension, otherwise they should be implanted in the abdominal cavity in order to preserve their endocrine function.

J. H. McCracken, Jr. (Texas State J M 26 564 (Dec.) 1930) reports on approximately 400 **fascial repairs** for hernia which he says seem indicated in the following types of cases: (1) direct inguinal hernia; (2) oblique inguinal hernia, with a sagging posterior wall, in patients past middle age; (3) femoral hernia in which the suture is used to



close the entrance of the femoral ring through the inguinal incision, (4) all recurrent hernias, and (5) all ventral hernias, including umbilical and epigastric. The sutures are taken from the fascia lata of the thigh, each being one-fourth inch wide and as long as the particular thigh will allow. They are threaded on a special needle and used as ordinary sutures in doing the plastic repair. One direct hernia recurred at the end of one year, in a case of double recurrent hernia there was recurrence on one side 15 months after operation.

W. E. Gallie and A. B. LeMesurier (Canad. M. J. 23: 165 (Aug.) 1930) in commenting on their results with living suture technic, state that the known failures are 6, in nearly 200 operations. In 1 case a recurrence which developed within 10 days showed that it is very important to secure the ends of the fascial strips with fine silk. In direct herniæ in which the sutures must bear the brunt of the strain of the spaces between, the sutures must be small to prevent protrusions. One of the failures reviewed was due to infection. In many of the cases the correction of the hernia was extremely difficult and would have been impossible by any other method. The authors have deviated little from their original technic.

J. J. Hepburn (New England Med. 204: 1035 (May 14) 1931) uses a **plastic reconstruction of the abdominal wall** in the treatment of *postoperative ventral hernia*. The success of the author's method depends on isolation of firm strong fascia on both sides of the hernia. The author has operated upon 115 cases of postoperative hernia with the above mentioned technic without mortality and with 4 small recurrences. His results are certainly most encouraging and compare favorably with others.

**HERPES ZOSTER.**—Herpes zoster occurring in midlife may be confused with *coronary sclerosis*, according to A. E. Parsonnet and A. S. Hyman (Ann. Int. Med. 3: 883 (Mar.) 1930). Mackenzie has pointed out that herpes zoster developing as a result of ganglionic disturbance of the first 4 upper thoracic segments of the spinal cord may resemble in every respect the rather characteristic syndrome seen in true angina pectoris.

Some authors have stated that the 2 diseases are of the same etiological background, while others believe that angina pectoris may be the result of herpes zoster itself. Herpes zoster sometimes follows angina pectoris.

Angina pectoris of the neurogenic type must be sharply differentiated from the anginal seizures which are the result of stenocardia, whether of the functional or of the degenerative coronary arterial type. In this latter group considerable pathology of the heart is usually found, such as coronary thrombosis, myocardial infarction and aneurism. Angina pectoris of the neurogenic type presents no such heart changes. Indeed, the heart may be entirely normal.

Three cases of angina associated with and preceded by herpes zoster are cited. The close resemblance between the pain of herpes zoster and that experienced in certain types of angina pectoris is striking. All patients remark on the similarity of symptoms. Two of them could hardly distinguish the difference.

In the 3 cases described, the coronary degenerative changes which took place following the herpes zoster attacks were rapidly progressive and ended fatally within 5 years. In each of these it seemed likely that the herpes zoster was the cause, since it occurred at a time when the heart was still normal.

Whether the pain component of the herpes zoster syndrome and that of angina pectoris is the same, or whether they are 2 distinct entities, using the same pathways for their transmissions, is a problem

Herpes zoster and angina pectoris exhibit identical zonal areas of altered skin sensitivity. There is a possibility of common etiological background in both herpes zoster and angina pectoris of the neurogenic type

J. M. A. Lowson (Brit M J 2 1157 (Dec 21) 1929) has recently drawn attention to an apparent connection between *herpes zoster* and *varicella*, and several correspondents have recorded cases in which herpes in one member of a family had occurred almost at the same time as varicella in another. Although cases of the 2 diseases coexisting have been described, the onset is, as a rule, not simultaneous, and, therefore, the author feels that the following notes may be of interest

A male Chinese, aged 36, was admitted to Tan Tock Seng Hospital on August 5, 1929, complaining of a painful eruption on the left buttock and inguinal region of 3 days' duration

On examination he was found to have herpes zoster affecting the above-mentioned sites, the posterior root ganglia of the last thoracic and first lumbar nerves being implicated. In addition, there were varicella vesicles, in varying stages of development, on the trunk and face. The patient had tried the effect of some Chinese medicine on the buttock, and this had caused several bullæ to appear.

C. C. B. Gilmour, of the Middleton Hospital for Infectious Diseases, in Singapore, states that about 6 months ago he saw an instance of the coexistence of the 2 diseases in one patient. In

this case the herpes affected the right side of the chest and axilla, while the varicella vesicles were much more numerous than seen in other patients

**TREATMENT.**—A report has been made by E. Wood Ruggles (Arch Dermat and Syph 23 472 (Mar) 1931) of a number of cases of herpes zoster which have been specifically benefited by sodium iodide administered intravenously. The following indicate the type of cases treated

The first case was a man, aged 30, who had a severe attack of herpes zoster, involving the right side of the face, chin, neck and ear, and extending half way to the vertex in the scalp. He was suffering from excruciating neuralgic pain. Sodium iodide, 2 Gm (30 grains), was injected intravenously, after which the patient returned the next day amazingly improved. The severe pain had practically disappeared, and the vesicles were flattened and beginning to desiccate. The treatment was repeated and 2 days later a third injection was administered. At the fourth treatment, 3 days later, the vesicles had dried and there was no serum and no pain. The skin was practically normal within 2½ weeks

The second case, a man aged 31 years, presented the following history. Five days previous to presentation he had severe neuralgic pain in the left side of the forehead, which was followed the next day by the appearance of several vesicles. The eruption extended to the whole left side of the forehead and into the scalp, and at his first visit there were also about 20 vesicles on the upper lid, the side of the nose and anterior to the ear, the latter area being considerably swollen. The following day the vesicles were somewhat flattened and the edema had vanished, but the pain was still

severe. On the fourth day, while the lesions had improved, the pain still persisted. There was moderate conjunctivitis, and the patient had had nausea and vomited. Sodium iodide was again administered and the next day the pain suddenly lessened. On the seventh day there was practically no pain, and the skin was greatly improved, but there was some pus under several crusts. Three days later he showed great improvement. All crusts were removed—a few black ones showed that gangrene had occurred—2½ per cent ammoniated mercury ointment was prescribed for the suppurating areas. Three days later 2 lesions had not quite healed, and he still had occasional mild neuralgic pains. He was, therefore, given the fifth injection, when rapid improvement occurred, the pains ceased and the skin became normal within 16 days after his first visit.

The author cites 4 orbital cases, involving the ophthalmic nerve, and in these apprehension is always felt concerning extension of the disease to the eye itself, with probable loss of vision.

Two of the patients had slight malaise following the first injection. In 1 case it is uncertain whether the fever should be attributed to the treatment or to the infection.

The method of treatment followed by the author has been to administer a 20 c c (5 dram) ampoule containing 2 Gm (30 grains) of sodium iodide, on the first, second, fourth and seventh days. Two patients received only 2 injections, 4, only 3. All of the cases cleared up in from 10 to 17 days.

In all of the cases, except the seventh, he employed quartz light and a dusting powder consisting of zinc oxide, ½ ounce (15 Gm); camphor powder 1½ drams (6 Gm.); cornstarch, 1 ounce

(30 Gm.), and morphine sulphate, 3 grains (0.2 Gm.).

The writer does not claim any originality for the discovery of this treatment, only its rediscovery, and states:

"As to the rationale of the treatment, I shall not attempt to be dogmatic. The ordinary effects of the iodides are not germicidal, they are supposed to cause lysis and release bacteria and to promote resolution of diseased tissues. However, in some conditions, especially when administered intravenously, they appear to have a direct action, e. g., in blastomycosis, actinomycosis and sporotrichosis, for which they are true specifics, and in gonorrheal epididymitis and rheumatism."

#### HERPES ZOSTER OPHTHALMICUS. See CORNEA

**HETEROPHORIA.**—In a discussion of Bell's phenomenon and the inverse Bell's phenomenon S. V. Abraham (Am J Ophth 14 656 (July) 1931) reports a large number of cases of normal persons who presented the normal Bell's phenomenon on closing the eyes, but upon forcible retraction of the upper lid exhibited the inverse phenomenon. He, therefore, concludes that both phenomena are merely instinctive protective reflexes. He also observed that after occluding 1 eye of a large number of normal patients, a majority exhibited hyperphoria of the occluded eye. He considers this a manifestation of Bell's phenomenon and believes that the occlusion test is misleading in examination for heterophoria.

L. F. Appleman (*Ibid* 14 36 (Jan) 1931) discovered from 0.75 to 3.00 degrees of hyperphoria in 253 out of 500 cases in which primarily no hyperphoria was shown at a distance. His method

is as follows. After making the usual test with the Maddox rod for distance, the dot-and-line test of Graefe is used at the reading distance, and the amount of prism required to adjust for hyperphoria at the near range is left before the eye while the distance test is repeated, any overcorrection for distance thus disclosed being reduced  $\frac{1}{2}$  degree at a time, but requiring the patient to continue to look through each successive prism until the next is in place.

He emphasizes 3 important determinations which are necessary to relieve symptoms by correcting lenses: (1) Refraction under a cycloplegic up to the age of 50; (2) a careful search for heterophoria, especially hyperphoria, (3) an estimation of the vergence power and detection of any convergence insufficiency.

### HIRSCHSPRUNG'S DISEASE.

See COLON MEGACOLON

### HISTOPLASMOSIS WITHOUT SPLENOMEGALY. — R. M.

Crumrine and J. F. Kessel (Am J Trop Med 11:435 (Nov) 1931) report the second case of histoplasmosis in this country, and the fifth in medical literature. This case differs from the 4 cases previously described in that the spleen was not enlarged sufficiently to be palpated, a constant finding in the other cases, and the fungus was found in this case to have a large, extracellular phase, in addition to the minute, intracellular form previously described in the other cases. The extracellular form was from 2 to 5 microns in diameter, surrounded by a halo believed to be a mucinoid capsule, the diameter of which was occasionally as large as 10 or 12 microns. It was found only in the spleen, whereas the small intracellular form was found in great numbers within

the large endothelial cells of the spleen, lymph nodes, lungs, liver and intestines.

The disease simulates tuberculosis of the mesenteric lymph nodes, together with ulcerative colitis, but smears at autopsy show no acid-fast bacilli. *Histoplasma capsulatum* of Darling, a fungus, is the infecting organism, and is found, as previously stated, packed in phagocytic cells in the spleen, lymph nodes, lungs, liver and intestine, with a large extracellular form in the spleen.

The case ran an 8 months' course to a fatal termination. It was characterized clinically by progressive emaciation, abdominal pain, weakness, cough and persistent diarrhea, with temperature rise from 99° F (37.2° C) in the daytime to about 101° F (38.3° C) in the evening. The stools were usually 8 to 10 a day, rarely only 2 or 3 daily.

One month prior to death an abdominal mass, the size and shape of a fist and wrist, was noted in the upper left abdomen, the lower pole of the mass on a level with the umbilicus, the mass being just to the left of the midline. It was nodular, not tender, and suggested a group of enlarged lymph nodes. At autopsy these nodes were found to be swollen, enlarged, caseous, but none were broken down.

The spleen was never palpated during the patient's 2 months hospitalization, which terminated in his death, and at autopsy it weighed only 210 grams (7 ounces) and measured 12 by 8.5 by 4 cm, which is very slight enlargement. Section revealed white nodules of 5 mm diameter, distributed through soft red pulp.

The *intestinal tract* was ulcerated from just above the anus through the rectum, colon and ileum. The ulceration consisted of 25 or 30 large ulcers, 1 to 2 cm in diameter, with red, undermined

edges, and complete destruction of the mucosa within the crater. There was no tendency to perforation, and the external appearance of the intestines was normal. There were approximately 50 smaller ulcers, about 4 mm in diameter. These showed a red border and a yellowish center of necrotic mucosa. The ulcers were discrete, and did not show the tunneling or tendency to confluence, which are so marked in the ulcers of *Endameba histolytica* infection.

Two *microscopic examinations* of the stools showed numerous yeasts. No attempt was made to culture the yeasts in the feces, as the nature of the disease was not suspected prior to the autopsy, and the presence of yeasts in large numbers aroused no suspicions, since *Blastocystis* and other nonpathogenic intestinal yeasts are often found in normal stools.

Attempts to culture the organism from the lesions at postmortem were unsuccessful, as were the efforts of Darling, Riley and Watson with the 4 cases of this disease previously reported.

Staining of the organism is satisfactorily accomplished with hematoxylin and eosin, iron-hematoxylin and eosin-methylene blue.

**HODGKIN'S DISEASE.**—Isaac Levin (J. A. M. A. 96:421 (Feb. 7) 1931) takes up a much discussed point and concludes that Hodgkin's disease (lymphoma malignum) and lymphosarcoma are nearly identical in their clinical manifestations. As compared with the general group of carcinoma and sarcoma, these conditions represent a special type of malignancy. The peculiarities in tissue structure and clinical manifestations of Hodgkin's disease depend not so much on the difference in causation, as on the special character of

the structure and function of lymphoid tissue.

Morphologically, Hodgkin's resembles an inflammatory granuloma rather than a malignant tumor. The clinical course sets it apart from any known parasitic or inflammatory disease. The author believes that both lymphosarcoma and malignant lymphoma begin as purely local conditions in one lymph node. In this lymph node either the lymphocytes or the reticulum cells, or both, acquire the characteristics of a cancer cell. Since these cells are very mobile, they are immediately transported into other regions throughout the organism. It is not difficult to conceive further that these transported lymphoid tissue cells find proper medium for their multiplication and development only within the lymphoid tissue of other regions or organs (lymph nodes, spleen, bone-marrow). In such regions the secondary metastatic tumors develop.

Both lymphoma malignum and lymphosarcoma frequently show tumors in parenchymatous organs which resemble in every particular metastatic tumors of carcinoma and sarcoma. Lymphocytes circulating in the blood are most readily influenced by radium and x-rays, while all other normal types of leukocytes and the erythrocytes possess a greater resistance. Normal lymphoid tissue is much less radio-sensitive than the various types of hyperplasias of lymphoid tissues. Simple inflammatory hyperplasias are less radio-sensitive than the neoplastic hyperplasias. The lymphoid tumors of lymphoma malignum and lymphosarcoma represent the most radio-sensitive of all tissues. The prompt beneficial therapeutic action of radiotherapy on lymphoma malignum is the best proof that biologically this is a neoplastic condition and more akin to

lymphosarcoma than to an infectious lymphoma. In the original article a series of case reports are included.

### HYDATIDIFORM MOLE.—

E. Novak and A. K. Koff (Am J Obst and Gynec 20:481 (Oct) 1930) report 2 cases of hydatidiform mole and 2 cases of chorionepithelioma, in all of whom the ovaries were available for study, while in 1 patient with chorionepithelioma, a histologic study of the pituitary gland was also made. The association of ovarian cystic tumors, otherwise termed theca-lutein cysts, with hydatidiform mole and chorionepithelioma is of particular interest to the gynecologist.

These investigators believe that the anterior pituitary gland is responsible for the lutein hyperactivity observed in the ovaries and that this hyperluteinization affects both the granulosa and the theca-interna.

The histologic examination of the anterior pituitary in the case of chorionepithelioma revealed an abnormal pregnancy reaction and explains why the biologic test for pregnancy remains positive long after the removal of the primary uterine tumor. They believe this reaction is due to the persistence of trophoblastic tissue in the metastases which is responsible for the pituitary reaction which, in turn, produces the abnormal ovarian response.

### HYDROCEPHALUS, OTITIC.

—**DEFINITION.**—C. P. Symonds (Brain 54:55 (Apr) 1931) has applied the term *otitic hydrocephalus* to a state of increased intracranial pressure which sometimes occurs as a complication of otitis media. The term *serous meningitis* which has previously been employed for the condition is objectionable, since

in these patients there is no clinical nor serologic evidence of actual inflammation of the meninges.

**ETIOLOGY.**—This is rather obscure. The condition may occur as a complication of an acute or chronic *otitis media* with or without *mastoiditis*, *labyrinthitis*, *lateral sinus thrombosis*, *extradural abscess*, or *meningitis*. Age seems to be a predisposing factor, since otitic hydrocephalus appears to be almost confined to children and adolescents.

**PATHOLOGY.**—This is also obscure, although there seems to be some evidence that either an excessive secretion or defective absorption is the basis of the condition.

**SYMPTOMATOLOGY.**—The onset may be insidious or there may be a preliminary phase of *fever* and *rigidity of the neck*. In the latter case, the symptoms of meningitis subside as those of hydrocephalus develop. *Papilledema* and intermittent *headache* are the most constant symptoms in the fully-developed state of otitic hydrocephalus. The headache is generalized or occipitofrontal, and of a "bursting" type. It may be of severe or slight degree, and in the latter case papilledema may advance to secondary optic atrophy without any other symptom of importance. *Nausea* and *vomiting* are inconstant. The temperature and the pulse rate are normal. *Drowsiness* is continuously present.

The *cerebrospinal fluid* is under increased pressure, but is clear and contains no increase in cells nor in protein. In those patients with a preliminary stage of meningitis, the cerebrospinal fluid examined during that phase contains an excess of cells and protein.

**COURSE AND PROGNOSIS.**—The illness may be protracted to weeks



or months, but recovery follows. However, impairment of vision due to optic atrophy may be a *sequel*.

**TREATMENT.**—Although in some cases recovery appears to have been spontaneous, the rational line of treatment is drainage of the excessive cerebrospinal fluid by lumbar puncture. This should be repeated if necessary, the indications being recurrent headache

or persistent papilledema. If repeated lumbar punctures fail to relieve the symptoms, **ventricular puncture** should be undertaken, in the first place on the right whichever the side of the aural lesion; if this fails, the left ventricle should also be punctured. Surgical attention should also be directed to the ear and its complications, in addition to the above mentioned procedures.

## I

**INFANT FEEDING.—BREAST FEEDING.**—A recent study by H. K. Faber and T. L. Sutton (*Am. J. Dis. Child.* 40:1163 (Dec.) 1930) has led them to conclude that there is no harm in weaning infants at the age of 3 months, provided that the circumstances are ideal and a suitable bottle feeding is provided. One series of 42 infants who had been breast-fed and another group of 42 infants who had received a cow's milk formula since birth were compared in respect to the gain in weight and frequency of infection. During the first 12 weeks of the infants' lives, the breast-fed babies had made a gain in weight which was 22 per cent greater than the average gain by the bottle-fed ones. Subsequently, however, over a period of 9 months, the infants given artificial feedings gained more weight and had fewer infections.

On the other hand, there are certain localities where infants are nursed until well into the second year of their lives. The observations of H. W. Pooler (*Arch. Pediat.* 47:698 (Nov.) 1930) indicate that no harm results from the prolongation of the nursing period, providing the health of the mother is good and the infant is thriving. In his territory of Derbyshire,

Eng., 27.6 per cent of 500 infants were partly or entirely dependent on the breast for milk after 12 months of age and their weights were above the average of other infants in that district who had been weaned earlier. Both groups had been receiving various solid food since the age of 6 months. An analysis of the breast milk of 11 mothers who had been nursing their infants for more than a year gave no evidence of a reduction of the fat, protein or sugar content and, in fact, in the majority of instances the fat content was above the average.

The same author tabulated the reasons for the *early weaning* of infants (*Brit. J. Child. Dis.* 27:269 (Oct.-Dec.) 1930). Of a group of 2285 infants, 4.3 per cent had been taken off the breast before the end of 4 weeks and this figure does not include the illegitimate or sick infants. The reason for weaning in 63 per cent of the instances was an insufficient milk supply, which was normal until the mothers got up from bed after their confinements and assumed household duties and worries again. Other reasons for early weaning were malformations or infections of the nipples, weakness of certain immature infants, and irregular nursing intervals, which

caused digestive upsets in the babies with a consequent substitution of breast milk with artificial formulas

A similar study of the reasons for *early weaning* was made of 200 infants observed in an out-patient dispensary and of 200 infants in private practice, by J Garland and M B Rich (New England J Med 203 1279 (Dec 25) 1930) The infants of the more prosperous families had been weaned at a much earlier age than the dispensary group Again, it was noted that the most common reason given for taking the child off the breast was the lack of a sufficient amount of milk The next most common reasons were illness of the mother and infection of the nipples Only 27 per cent of the infants seen in private practice had been nursed for more than 5 months while 51.5 per cent of the clinic patients had continued nursing for longer than that time The desire and ability of the mother to nurse her infant appeared to be the factors deciding the duration of time of breast-feeding

The constituents of breast milk are determined to some extent by the *diet of the mother* This fact has been repeatedly claimed in the last few years and especially in regard to vitamins Sufficient vitamin B in the diet of the mother leads to the secretion in the milk of vitamin B and also amounts of vitamin D This knowledge led A F Hess, J M. Lewis, F. L. McLeod and B. H. Thomas (J. A. M. A 97:370 (Aug 8) 1931) to investigate the vitamin D content of the milk of cows fed irradiated yeast and irradiated ergosterol. The milk was found to contain enough vitamin D to protect infants against rickets Irradiated yeast diet caused the secretion of more vitamin D than did the irradiated ergosterol

The *iron content of breast milk* is too low to supply the needs of infants over long periods of time However, the supply of this mineral varies considerably with age and diet, according to H Dorlencourt and Mme Calugareanu-Nandris (Nourrisson 17 227 (July) 1929) Mothers between the ages of 20 and 40 years have a higher iron content in their milk than mothers at the extremes of the child-bearing age Large amounts of iron salts taken by mouth increased the secretion of iron in the breast milk and the authors suggested the administration of this mineral to mothers of anemic infants as one method of treatment

**COW'S MILK.**—During the last few years there has been a tendency to give infants more concentrated foods and to be more lenient in the amounts given Unlimited amounts of 2 milk formulas were offered to 2 groups of infants and the results reported by G. F Weinfeld and F B Floore (Am J Dis Child 40 1208 (Dec) 1930) One group of 39 infants was given a concentrated feeding of whole milk with 8 per cent added dextrimaltose and the other group of the same number was given a more dilute feeding of milk (22 oz—660 c c), water (4 oz—120 c c.) and dextri-maltose (2 oz—60 c c—of a 50 per cent solution). The bottles were offered at regular intervals and the infants allowed to take as much of the formula as they wished. Similar milk formulas were offered in unlimited amounts as complementary feedings to nursing infants Both foods were tolerated well The infants given the dilute mixture took larger quantities than those given the concentrated food, but the caloric intake of the latter group was larger, which indicated that the amount of food voluntarily taken by an

infant does not depend entirely on the physiologic capacity of his stomach, but probably this factor, together with his caloric requirements, determines the amount of food needed. It was an interesting observation in this study and somewhat contrary to the usual experience that during attacks of diarrhea and of certain parenteral infections, the infants continued to take large amounts of milk offered to them and as a rule continued to gain weight.

A similar experiment was conducted by H. P. Wright, A. K. Geddes and C. L. Vick (*Am J Dis Child* 40:927 (Oct) 1930). Unlimited amounts of 2 types of milk were offered to infants at regular intervals. One formula contained lactic-acid milk and the other sweet milk and the sugar content of each was increased 5 per cent by the addition of corn syrup. Five regular feedings were offered each day and the infants allowed to take as much of the formula as they desired. When they began taking 32 ounces (960 cc) of milk daily, cereal and vegetable broth were added to the diet and the number of feedings reduced to 4 a day. The average age at which this latter procedure was instituted was 4 months. All of the infants made good gains in weight. It was the impression of the investigators that the infants on the sweet milk mixture suffered from mild digestive disorders more frequently than those on the acid-milk, but in general there were no marked differences in the 2 groups.

An intensive study of 9 infants on a concentrated diet of undiluted cow's milk to which 6 per cent sugar had been added in the form of corn syrup, convinced M. van K. Nelson (*Am J Dis. Child* 39:701 (Apr) 1930) that such a food was not only safe but very beneficial. The average increases in

length and weight of these infants was greater than that of the averages computed for infants on dilute milk mixtures. The group receiving the concentrated feedings also had a greater nitrogen retention per kilogram of body weight and the percentage of intake also was greater than in control groups taking dilute feedings.

Another reason for the use of **more concentrated feedings** for infants is the need of certain mineral elements in the diet to provide for normal growth and development. The experiments of E. L. Samuel and I. N. Kugelmass (*Am J Dis Child* 39:687 (Apr) 1930) demonstrated that in animals fed with acid-forming diets, the blood changed to the acid side, while base-forming diets changed it to the base side. With the latter diet, metabolism and growth was much greater. According to the investigators the conclusions of these results could be applied to infant feeding at certain critical times, such as the transition from breast feeding to cow's milk formulas. If the milk is diluted and only refined cereals are given in addition, there may be a definite deficiency of the base elements. More concentrated foods were recommended, together with the use of fruit and **vegetable juices** or **pureés** which contained sufficient quantities of minerals.

The type of sugar which is best absorbed by the infant was studied from the standpoint of blood-sugar determinations by H. M. Greenwald and S. Pennell (*Am J Dis Child* 39:493 (Mar) 1930). The first blood sugar which served as an indication of the fasting level was taken 3 hours after a meal. Then a solution containing either *dextrose*, *lactose*, *saccharose* or *dextrin-maltose* was given by mouth. Two

grams (30 grams) of the sugar were given for each kilogram ( $2\frac{1}{5}$  pounds) of body weight. Blood sugar determinations were made in the following  $\frac{1}{2}$  hour, 1 hour and 2 hours and the rate of absorption and the tolerance were judged from the results. The age of the patients ranged from 2 to 10 days, and there were 15 in each group. The best rate of absorption followed the administration of dextrose, while saccharose and lactose followed in the order named. The blood sugar curves obtained from the giving of dextrin-maltose were very irregular and no definite conclusions could be drawn from them. When similar sugar tolerance determinations were made in infants who were on the breast, the lactose as it occurred in breast milk was observed to have a higher rate of absorption than any of the above sugars given in water solution.

The effect of the sugar in an infant's feeding on the total weight and the acid content of its stools has been the subject of an investigation by J. R. Gerstley, C. C. Wang and A. A. Wood (*Am J Dis Child* 39:487 (Mar) 1930). When the diet of an infant is changed from breast nursing to a cow's milk diet, there is a decrease in the sugar of the milk from 7 per cent to 4 per cent. When such a change of diet takes place, the total acidity of the stools increases, the lactic acid diminishes in amount and there is an increase in acetic and propionic acids. Although the amount of lactose in breast milk is greater than in cow's milk, there was a decreased output of lactic acid in the stools, which suggested to the investigators that the absorption of lactose in the intestinal tract had a greater influence on the lactic acid output than certain other factors, such as bacterial de-

composition. In a subsequent experiment the same investigators (*Ibid.* 39:729 (Apr) 1930) studied the effect of adding larger amounts of lactose to cow's milk feedings. One series of infants were given milk formulas with 3 per cent added lactose and another group 12 per cent added lactose. The addition of sugar caused an increase in the amount of volatile acid in the stools and the 12 per cent lactose addition caused a diminution of the weight of the stools. In no instances, however, did diarrhea occur. Therefore, the mere increase of certain acids in the stools as the result of a diet high in carbohydrate could not be considered as the etiology of diarrhea. The latter condition probably is dependent on some general disturbance of body nutrition.

**CONDENSED MILK.**—There has been considerable adverse criticism of the continued use of proprietary sweetened condensed milks in the feeding of infants. However, such a milk was employed as food for a group of 50 infants between the ages of 3 weeks and 5 months and, according to A. G. De Sanctis and J. D. Craig (*Arch Pediat* 48:439 (July) 1931), very favorable results were obtained. There were satisfactory gains of weight, and the physical and mental development was apparently normal. No evidence of secondary anemia occurred and infections were no more common in this group of infants than in others fed on different diets. The advantages of this type of feeding seemed to be (1) its ready digestibility, partly due, no doubt, to the small soft curds which were formed in the stomach; (2) its low bacterial content, and (3) the presence of the vitamins A and B, and (4) its sufficiency in caloric and nutritional requirements. (The objections of other

clinicians to this type of sweetened, condensed milk have been its high carbohydrate content in relation to the protein and fat, with the result that in usually employed dilutions which adjust the carbohydrate percentage to normal figures, the protein content is very low. Over long periods of time, therefore, this feeding would not furnish the body tissues with sufficient nitrogen and essential amino-acids.)

**ACID-MILKS.**—Numerous clinical investigations during the last year have given approval to the value of acid-milks in the feeding of infants. To acidify milk, *lactic acid* is used most commonly, but *orange juice*, *lemon juice* and *hydrochloric acid* have proven very satisfactory. *Citric acid* has been employed by J. E. Gonce, Jr. and H. L. Templeton (*Am J Dis Child* 39:265 (Feb.) 1930) and they state that its advantages over lactic acid lie in its ability to accomplish all that lactic acid does and yet it is better tolerated by the infant and is more accessible for use in the average home. They employed proportions of 4 Gm. (1 dram) of dried citric acid to a quart (1000 cc) of boiled milk, which produced an acidity with an average pH of 4.8. When this milk was fed to 35 infants and withdrawn from the stomach shortly afterwards, the curds were found to be very small, discrete and of a soft consistency. The pH of the stomach contents was similar to that obtained with lactic-acid milk feedings. The stools of the patients on the citric acid milk were well digested, smooth and firm; the urine gave no evidence of a toxic effect of the acid on the kidneys. This milk was fed to a group of 50 infants with various diseases in a hospital and 92 per cent. gained weight, 4 per cent. remained stationary, and 4 lost weight. Nineteen

infants living at home were given the same feeding and made good gains in weight. These results were thought to be more favorable than the average of those obtained with other types of milk.

**OTHER FOODS.**—The recent popularity of **bananas** as a food for infants with certain digestive disturbances has led to the production of a **powdered** product which eliminates certain difficulties connected with the feeding of this food, according to S. V. Haas (*Arch Pediat* 48:248 (Apr.) 1931). (1) Ripe bananas are not available at all seasons of the year, (2) exact quantities must be measured at each feeding, and (3) the method of making a proper pulp which can be given through a nipple is difficult and laborious. The dried product contains 84.71 per cent carbohydrate, 4.86 per cent protein, 1.5 per cent fat, 3.25 per cent fiber and cellulose, 3.18 per cent ash, and 2.5 per cent water. The vitamins A, B, and C are said to be retained. The powder mixes well with water or milk and may be used as a substitute for sugar in milk formulas. The product was employed in the feeding of 41 infants and was readily digested, and all the patients gained more rapidly in length than an average group but the gain in weight corresponded to the normal.

The value of **gelatin** in milk formulas lies in its use as a substitution of certain milk proteins towards which an infant may be allergic, or as an addition to milk to concentrate the feeding. This is the opinion of T. O. Elterich, D. H. Boyd and A. Neff (*Arch Pediat* 47:286 (May) 1930), who observed its use in the feeding of 11 infants. The addition of 4 tablespoonfuls of gelatin to a milk formula does not increase the total volume and adds 100 calories to the mixture. It was well tolerated,

there were no instances of "protein fever" (which has been observed in infants on high protein diets) and the gain in weight was in accordance to the added caloric value of the food. Although gelatin is known to be an incomplete protein food in that it lacks certain essential amino acids, it may be used for short periods of time as a substitute for certain proteins of milk to which an infant is sensitive.

**INFANT MORTALITY.—RATE.**—In 1929, the United States experienced the lowest infant mortality rate of any year since the beginning of systematic recording of infant deaths by states in 1915. These figures, compiled by the Division of Vital Statistics of the United States Department of Commerce, indicate that there was a drop of 1 per cent from the preceding year. However, there was also a decrease in the birth-rate during the year of 1929. For the sixth consecutive year the state of Oregon had the lowest infant death rate. The highest figures occurred in some of the southern states, which is to be attributed to the large negro population. A. L. Stoughton and M. Gover (Pub. Health Rep. 44.2705 (Nov. 8) 1929) call attention to the fact that the infant mortality rate is higher in the colored race than in the white in every locality and is highest in the urban centers of the South.

The infant death rate has also decreased in many European countries in the last 2 years. During 1930, England had the lowest infant mortality rate ever recorded there—11.4 deaths per 1000 live births (London Correspondent J. A. M. A. 96.1244 (Apr. 11) 1931). In the Oriental countries, India had an increase in the infant death rate but several other countries had decreases,

notably Japan. The rate in Tokyo during the months of January to September, 1929, was 12.5 per 1000 and for the same months in the rest of Japan 14.4 per 1000.

**CAUSES**—In respect to the chief causes of death in infants, an interesting study of 800 autopsies of infants dying within the first month of life has been made by J. N. Cruickshank (Med. Research Council Report, 145, 1930). The 3 most frequent causes of death of this group of patients were (1) conditions produced by birth asphyxia, birth injury or prematurity, 67.5 per cent, (2) infections of various natures, 29.75 per cent, and (3) gross developmental defects which accounted for 2.75 per cent.

H. C. Stuart (New England J. Med. 204.149 (Jan. 22) 1931) reports an investigation of fetal and neonatal deaths in Boston during the year 1929. Miscarriages and abortions which occurred before the development of a viable fetus, *i. e.*, pregnancies less than 24 weeks' duration, were excluded. Of 650 infant deaths, 264 were dead at birth, 312 died within the first 2 weeks after delivery, 74 died later than 2 weeks and before 1 year of age. The cause of death of 139 infants was some disease of the mother. Of these diseases toxemia, eclampsia and nephritis were the most common (43 patients), local uterine disturbances such as placental infarcts, fibroids, etc., occurred in 27 patients, accidents in 73 and respiratory diseases in 12. Of the deaths due to infant diseases, 135 were undiagnosed, 122 were caused by malformations of the infant; and 99 by congenital defects. The toxemias of pregnancy were the most common maternal causes of infant death, while placenta previa and premature separation of the placenta were



most frequent causes of infant death during delivery. Twenty-five per cent of deaths had no assigned cause. The author concludes that good care during labor will have effect on only about a third of the infant deaths. Good prenatal care is a very important factor in reducing the other two-thirds.

S. Peller (*Zentralbl f Gynak* 55:268 (Jan 31) 1931) likewise emphasizes the importance of the maternal health during pregnancy in influencing a lowering of the infant mortality rate. To the unfavorable living conditions of the mother he attributes many premature deliveries and also small underdeveloped fetuses, who usually die soon after birth.

P. Lereboullet (*Paris méd* 2:436 (Nov 15) 1930) groups the chief causes of infant mortality under (1) the obstetrical difficulties, (2) gastroenteritis infections especially after the first months, and (3) the acute infectious diseases, including syphilis, tuberculosis, the respiratory diseases and the contagious diseases.

Taking into consideration the entire age group of children up to the age of 13 years, an interesting review of the necropsies of 1000 children was given by I. M. Epstein (*Am J Dis Child* 41:1363 (June) 1931). Pneumonia was the most frequent pathologic finding as the cause of death. Tuberculosis was second and in order of frequency there followed septicemia, congenital malformations, intoxication, purulent meningitis, contagious diseases, acquired heart disease, marasmus and peritonitis. During the first year alone, pneumonia, enteritis and congenital malformations caused most of the infant deaths.

**PROPHYLAXIS.**—The methods used for combating infant mortality in Switzerland have been described by P.

Guattier and A. Thevenod (*Le Nourrisson* 17:277 (Sept.) 1929). There the infant mortality rate has decreased from 15 per cent in 1900, to 8.4 per cent in 1920. Provision has been made for (1) the suppression of abortion; (2) legislation which provides for help to mothers for a few weeks before and after the birth of the children, and (3) a definite educational program has been instituted through the Red Cross, the infant hygiene dispensaries and the nurseries, for the girls of high school age and for young mothers. This program is somewhat similar to the recommendations of the report of the League of Nations committee (*Pub Health Rep* 44:2268 (Sept 20) 1929), which advised (1) education of the public in matters of hygiene, (2) education of physicians and midwives of the same principles, and (3) the employment of visiting nurses to supervise the care of newly-born infants.

The importance of a sanitary water and milk supply, and of good prenatal and obstetrical care in reducing the infant mortality rates is illustrated in recent reports from Chile and Argentina. G. A. Alfaro (*Bol Inst internat am de protec a la inf* 4:373, 1930; *Am J Dis Child* 42:936 (Oct.) 1931) and L. C. Mackenna (*Ibid* 4:426, 1930; *Ibid* 42:937 (Oct.) 1931) report very high infant mortality rates among rural portions of those countries, 120 to 260 deaths per 1000 live births in parts of Argentina and 267 to 274 in certain small cities of Chile, while in the large cities of Buenos Ayres and Santiago, the mortality of infants approximates the averages in cities of the United States and Europe. The causes of death of infants in the outlying districts of Argentina and Chile are chiefly gastroenteritis and respiratory diseases.

**INTESTINES.—FLATULENCE**—*Physiology*—A study of intestinal flatulence with regard to physiology, pathology and therapy was made by J. L. Kantor and J. A. Marks (Ann Int Med 3 403 (Nov) 1930). Physiologically, gas appears in the intestines from 2 sources according to these authors: (1) swallowed air, and (2) gas derived from food both from the interaction of acid gastric juice with alkaline duodenal contents and from bacterial action in the small and large bowel. Flatus is the resultant of air admixture, gas produced from food, gas absorption from the intestine and gas diffusion into the intestines. Its composition is given by Fries as follows:

	Per Cent
CO <sub>2</sub>	10.3
O <sub>2</sub>	0.7
CH <sub>4</sub>	29.6
N	29.4

Normally about 1 liter is passed by rectum daily.

**Etiology.**—Pathologically, the authors found that excessive flatulence was a chief complaint in about 33 per cent of 1496 private patients. The chief causes are outlined as follows:

**A. Excessive gas intake or production**

1. Aerophagia
2. Vegetable diet which favors decomposition of cellulose and starch in the cecum
3. Abnormal bowel flora, such as yeast and fermentative bacteria
4. Gas diffusion from the blood as occurs in cases of neurogenic and toxic ileus

**B. Deficient gas expulsion, seen in obstructive lesions**

**C. Deficient gas absorption, due to:**  
(1) interference of mucosal blood supply, as in volvulus, portal obstruction, mesenteric occlusion, general circulatory

failure, etc., (2) interference with mucosal integrity as in organic colitis, and (3) intestinal atony from nervous or toxic causes, allowing decreased intraintestinal pressure.

**Treatment** depends upon an accurate diagnosis of the cause. In the neurogenic types **sedation** and **relaxation by medication** and **heat** are indicated. *Aerophagia* must be controlled **psychologically**. **Excess cellulose** should be **avoided**. In *post-operative distention* the authors recommend **encouragement of belching**, use of **stomach and rectal tubes**, **enemata** and **pilocarpine**, **physostigmine**, or **pilocarpine** if needed.

**BACTERIAL HYPERSENSITIVITY OF THE INTESTINAL TRACT.**—S. E. Dorst and R. S. Morris (Am J M Sc 180 650 (Nov) 1930) studied 30 patients with colonic symptoms of long standing from the standpoint of sensitivity to organisms normally present in the bowel. Twenty-six of the 30 gave evidence of marked sensitivity to one or more organisms. In a series of "normals" tested, over 50 per cent failed to have any skin reaction to their bowel organisms. In the skin positive group a careful history revealed some gastrointestinal disturbance in all.

Vaccines made up from the bacteria causing skin reactions were administered in frequent small doses over varying periods. Subsequent skin tests revealed desensitization in most cases. As desensitization occurred, amelioration of symptoms was usually noted.

*In vitro* experiments with sodium ricinoleate, "Soricin," (derived from castor oil) revealed its ability to detoxify bacteria causing sensitivity reactions with the exception of *Streptococcus fecalis*. When given by mouth, this

drug resulted in desensitization of the patients, as judged by subsequent skin tests

**INTESTINAL PROTOZOA.**—A study for evidence of protozoan infestation in 52 patients in Baltimore was made by J. Andrews and M. Paulson (*Am J M Sc* 181:102 (Jan) 1931). They found an incidence of 10.9 per cent of infestation distributed as follows:

	Per Cent
<i>Endameba coli</i>	4.2
<i>Giardia lamblia</i>	2.7
<i>Endolimax nana</i>	2.5
<i>Trichomonas hominis</i>	2.1
<i>Iodameba williamsi</i>	1.3
<i>Chilomastix mesnili</i>	1.3
<i>Endameba histolytica</i>	0.2
<i>Embadoomonas intestinalis</i>	0.2

**TUBERCULOSIS.**—Records of ex-service men provided material for a statistical study of intestinal tuberculosis by P. B. Matz (*Ibid* 179:532 (Apr) 1930). Intestinal tuberculous lesions were found in 60.5 per cent of 200 patients dying from pulmonary tuberculosis. In 16.7 per cent. of those with intestinal lesions the intestinal involvement appeared within a year of the pulmonary symptoms, while 4.4 per cent showed bowel involvement in from 1 to 4 years.

The distribution of the intestinal lesions in 849 patients in order of frequency was as follows: cecum, ileum, ascending colon, transverse colon, ileocecal region, descending colon, jejunum, appendix, duodenum, rectum and sigmoid.

The x-ray pictures most frequently observed were filling defects in the cecum and descending colon (36.7 per cent of cases); an irregular cecum and loss of haustration in the ascending colon was seen in 29.6 per cent; hypermotility at 6 hours in 25.8 per cent, other filling

defects in the large bowel 17.1 per cent, ileal stasis and delayed cecal filling in 13.2 per cent, and fixation of the cecum in 3.2 per cent.

The most frequent lesions at autopsy were active ulcerations in 6.2 per cent, some active and some healed ulcerations in 1.7 per cent, and fibrosis in 0.7 per cent. Diagnosis was first made at autopsy in 12.6 per cent, 43.3 per cent had been diagnosed by clinical and x-ray methods.

**MUCOUS COLITIS.**—*Etiology.* After analyzing 500 cases of mucous colitis, J. Friedenwald, M. Feldman and L. J. Rosenthal (*Ann Int Med* 3:521 (Dec) 1929) came to the conclusion that the disease is purely neurogenic in origin and that any inflammation or ulceration present is superimposed on the neurogenic background. Contributing factors as found by these investigators were chronic constipation in 7.2 per cent, gastric dyspepsia in 6.4 per cent, visceroptosis in 5.8 per cent, abdominal adhesions in 3.7 per cent, focal infection in 2.3 per cent, chronic cholecystitis in 1.8 per cent, and chronic appendicitis in 1.3 per cent. Endocrinal disorders were demonstrated in 0.8 per cent. Only 1 per cent gave evidence of food allergy.

*Symptoms.*—The most common symptom was constipation, having been found in 7.2 per cent. Typical mucous colic occurred in 5.0 per cent, while 3.7 per cent had generalized abdominal discomfort. Ten per cent had alternating constipation and diarrhea, while in 0.9 per cent diarrhea alone was present. An analysis of gastric secretion revealed no consistent alteration. The results of their observations were as follows: normal secretion in 4.0 per cent, hyperacidity in 2.7 per cent and hypoacidity or anacidity in 3.2 per cent. The string sign by x-rays was present in 1.0 per cent.

**ULCERATIVE COLITIS.—**

**Etiology**—A survey of the psychogenic factors involved in 12 patients with ulcerative colitis has been carried out by C D Murray (Am J M Sc 180 239 (Aug) 1930). He draws the following conclusions. The outstanding trait of the 12 patients studied, beside fearfulness, is their emotional immaturity, and in this respect they differ from the gastric ulcer individuals who give the impression of a greater emotional development. Diarrhea is an infantile response to fear. Sexual problems were the most common immediate causes of attacks.

Referring to etiology Felsen (Arch Int Med 48:786 (Nov) 1931) states that idiopathic ulcerative colitis appears to be the result of a breakdown of the normal system structure and the local intestinal protective mechanism due to factors as yet unknown, plus a superimposed infection. The author believes that the intestinal flora in this disease differs from the normal quantitatively rather than qualitatively. He has seen streptococci of the type normally constituting a small minority of the colonic inhabitants increase until they could be obtained in pure culture with the exclusion of *Bacillus coli*.

**Complications.**—J A Barga (Ann Int Med 3 335 (Oct) 1929) has analyzed 268 complications occurring in 693 cases of chronic ulcerative colitis. Polyposis heads the list with an incidence of 10 per cent of the total series, stricture with 8.5 per cent, arthritis, 4.3 per cent, and perirectal abscess, 3.7 per cent. are next, with perforation, 2.6 per cent., skin lesions, 2.4 per cent; malignancy, 2.2 per cent, completing the list of the more frequent complications.

**Treatment.**—Treatment of ulcerative colitis by means of intestinal oxy-

genation has been suggested by Felsen (*loc cit*). Having previously found that strongly oxidizing agents used by means of colonic irrigations seemed to benefit cases of nonspecific ulcerative colitis, this writer used pure oxygen in 117 cases, including various types of the disease group as well as controls. The report is preliminary and does not attempt to give end-results.

In normal persons 1 liter (quart) of oxygen gas was found to be tolerated without discomfort. X-ray studies showed absorption of the gas within 6 hours. Patients with ulcerative colitis were given 250 c.c. ( $\frac{1}{2}$  pint) of oxygen alternate hours from 8 A.M. to 8 P.M. without undue discomfort or danger of perforation. The gas was given as slowly as possible.

According to this writer, clinical results were noted after from 2 to 7 days, usually beginning with a decrease in the foul odor of the stool, cessation of bleeding, improvement in the general condition and possibly fewer movements. Later the stools became more formed.

The results are believed due to the elimination of the spore-bearing anaerobes, and the encouragement of the superficial growth of obligatory or facultative aerobes. The former effect may decrease toxic symptoms, while the latter favors the discharge of aerobic bacteria in the form of pus, according to the authors. It is further suggested that this method of treatment stimulates mucosal metabolism and possibly its resistance to infection. Less extensive fibrosis seems to follow this type of treatment.

**ENTERECTOMY.—Pathologic Physiology.**—S Ishikawa (J Oriental Med 11 141 (Nov) 1929) has investigated the physiologic function,

especially that causing disturbance in the metabolism of an animal enterectomized to the point of just maintaining life, with the view that it may contribute to a better understanding of the physiology of the intestines. As a first step, the author investigated the general results after the operation and prognosis, and he here reports the results briefly. A dog can stand an excision of more than half the small intestine, and within a month or two, regain the same outward appearance as before the operation. An enterectomy of more than two-thirds of the intestine causes the dog to die gradually, or even suddenly without any particular pathogenesis which might incidentally lead to its death. The prognosis is dangerous even in one showing encouraging progress. The excision of an entire intestine, exclusive of the duodenum, is critical, as it causes an insufficient supply of nutrition, and the dog dies sooner or later, however, the animal may live for a certain period (100 days being the maximum observed). There is no difference in the upper or lower enterectomy as it affects the animal's outward appearance. The observable symptoms after the operation are thirst, hunger and diarrhea. The greater the excision, the more obvious the symptoms. The compensatory mechanism after the operation is considered to be quite automatic: the increase in the time required for absorption by the remaining intestine, and the quantity of food taken appear to affect the mechanism greatly. In the post-mortem of more than two-thirds of the enterectomized animals, marked anemia and atrophy were observed.

**INTESTINAL OBSTRUCTION, ACUTE.**—According to O. H. Wangersteen (Minnesota Med 14:16 (Jan) 1931), the mortality of the surgical

treatment of acute intestinal obstruction is as high today as it was 40 years ago. It rises with the delay of treatment. Statistics show that it increases from zero in cases treated within 6 hours after the onset of the symptoms to 40 per cent in cases in which treatment is delayed for 6 days.

Experiments performed by the author did not indicate that the contents of the obstructed loop of bowel are any more toxic than the contents of the normal bowel. However, if strangulation has occurred there is loss of vitality of the tissues involved and normal absorption takes place through the mesenteric vessels and from the serosa of the peritoneum. Studies of the blood reveal an increased combining power for carbon dioxide with a decrease of blood chlorides. The administration of normal salt solution will combat dehydration and prolong life. In strangulation, the use of saline solution is of no particular advantage. In obstruction of the lower bowel there is no change in the chemical character of the blood.

**Diagnosis.**—Early diagnosis is difficult because at first there are no local findings. The development of such signs as meteorism, collapse, and stercoraceous vomiting often means that the patient is beyond hope of cure by operation. Auscultation of the abdomen will reveal loud peristaltic rushes with a peculiar bubbling sound such as is produced when water is poured from a bottle. At times, a metallic tinkle may be heard. The use of the enema may be misleading, as gas and feces may be expelled from the distal bowel even when complete obstruction is present. The x-ray is of aid in the diagnosis since, in the case of adults, the visualization of gas in the small bowel is evidence of intestinal obstruction. The "ladder pat-

tern" and the presence of "fluid mirrors" make the diagnosis certain. Auscultation of the abdomen will differentiate between mechanical obstruction and the silent abdomen of intestinal paralysis. Any patient with intermittent colicky pain in the abdomen which is not relieved by enemas should be carefully observed for intestinal obstruction.

**Treatment.**—Operation should be performed as soon as it is reasonably evident that obstruction exists. The surgeon should not wait to determine the location or character of the obstruction. If the patient's condition permits, the ideal procedure consists in release of the obstruction, removal of the devitalized portion of bowel, and intestinal anastomosis. In an urgent case, strangulation of the bowel should be treated by exteriorization if resection is not advisable. In some cases otherwise inoperable, enterostomy of the bowel proximal to the obstruction is of great value. Jejunostomy is contraindicated on account of its mortality.

**INVAGINATION IN CHILDREN.**—*Etiology.*—W. Obadalek (Beitr. z. klin. Chir. 146:668, 1929) claims that an important rôle in the causation of invagination is played by dietetic errors, especially in nurslings, who are very sensitive to changes. Such errors account for the frequency of invagination in July. Every condition favoring disturbances of nutrition may cause invagination and probably spasmophilia. Trauma is of secondary importance.

**Diagnosis.**—Invagination is manifested in nearly every case by pain. Vomiting is seldom absent (6 in 53 cases). In 4 extreme cases of perforation peritonitis the vomiting was of the fecal type. Blood was found in the stools in 62 per cent of the cases and in

the enema water in 83 per cent. A mass was visible in fewer than 53 per cent, but was discovered on palpation under anesthesia in all. Visible peristalsis was noted in 22 cases and was always apparent when the abdomen was still soft and yielding. In the presence of meteorism, it was more difficult to demonstrate. The author ascribes great importance to the demonstration of free fluid in the abdominal cavity, which was possible in all of the cases reviewed as well as in other forms of mechanical ileus. He disapproves of x-ray diagnosis with the use of a contrast medium because of the associated loss of time and the possible injury that it may cause in infants.

**Differential Diagnosis.**—In the diagnosis it is most important to differentiate intestinal invagination from intoxication which may also be associated with apathy, vomiting, visible peristalsis, and the presence of blood in the stools. The latter can be ruled out by the absence of a tumor and of free fluid. Of the cases reviewed by the author, 40 per cent were admitted to the hospital with the diagnosis of intoxication. Other erroneous diagnoses were dysentery, cavernoma of the ileum, Barlow's disease, appendicitis, and purpura. The author erred in a case of sigmoiditis.

**Treatment.**—The author concludes that the best treatment of intestinal invagination is operation, regardless of the age of the patient or the type or duration of the condition.

**POSTOPERATIVE ILEUS.**—J. Brennan (New York State J. Med. 31:77 (Jan. 15) 1931) defines 2 main types of postoperative ileus, *i.e.*, the mechanical and paralytic. The former is due to such conditions as tumors, volvulus, and adhesions; the latter is insidious and is often overlooked.



show the same clinical course, with the symptom-complex of pain, tympanites, vomiting, and complete constipation, if left unrelieved by **enemas**, **stomach washings**, passing of the **duodenal tube**, and the administration of **sodium chloride**, the complication may compel further **surgical intervention**. High obstruction is rapidly fatal, the occurrence of fecal vomiting must be regarded not so much as a symptom of intestinal obstruction as one of approaching death, being too late for surgical cure. There is a similarity of symptoms between the terminal stages of ileus and death from shock or gas gangrene, the fatal termination is probably due to absorption of nucleoproteins from the degenerated intestinal lining, together with such factors as dehydration and loss of chlorides and alkalosis.

**Treatment** is largely preventive and necessitates a thorough knowledge of the patient beforehand, study of the blood chemistry, not too early catharsis, and a return to the normal water balance in the body, with, in certain selected cases, the performance of an ileostomy as part of the original operation. In late cases a jejunostomy relieves the toxicity best, and the intestinal contents are replaced with **sodium chloride solution**, 5 per cent intravenously and 3 per cent in large quantities subcutaneously.

#### INTRAVENOUS THERAPY.—

There has always been considerable hesitancy felt regarding intravenous injections because of the dire results occasionally seen. S. Hirshfeld, H. T. Hyman and J. J. Wanger (Arch Int Med. 47.259 (Feb) 1931) state that very often the shock, which is a common complication, is due to the speed of injection and that any molecule injected

rapidly into the venous system to cause this reaction. He believes this is the result of liver damage and that the same solutions given slowly would not cause such crises. A careful consideration of the speed of injection and of the strength of the solution injected would do away with many of the reactions seen during and after intravenous therapy.

E. B. Carter (J. Lab. and Clin. Med. 16.289 (Dec) 1930) gives a very good *test for the determination of pyrogens in distilled water* which is to be used in intravenous therapy. He takes 100 c.c. of distilled water in a sterile beaker, heats it to boiling, acidulates with 10 c.c. of dilute sulphuric acid and adds 0.1 c.c. of twentieth normal potassium permanganate. Carter states that continuous boiling for 10 minutes should not destroy the color of the solution and feels that this test should be carried out in all institutions where distilled water is being prepared for intravenous use.

#### IODIDES. — PHYSIOLOGICAL ACTION.—

From a statistical study of the effect of potassium iodide on the pulse rate of 34 normal patients, D. McEachern (Bull. Johns Hopkins Hosp. 47.299 (Nov) 1930) found that 12 showed a significant increase in the pulse rate, 5 a significant decrease, and in 17 there was very little change. When present, the changes came on gradually from the third to the seventh day and reached their maximum on about the tenth day. The rate returned to normal within a week after the drug was discontinued.

The effect of iodides was studied by D. McEachern and B. M. Baker, Jr. (Bull. Johns Hopkins Hosp. 47.304 (Nov) 1930) in 14 normal patients, 4 of whom were forced to drop out of the

experiment because of rather severe iodide reaction. The remaining 10 carried on the treatment for approximately 22 days. These were first given the compound solution of iodine but, because of its taste, this was soon changed to potassium iodide, which was given in doses graduated from 1 Gm (15 grains) daily during the first week, to 3 Gm (45 grains) daily during the third week. Electrocardiographs made on these patients showed no significant effect of the drug on the heart muscle.

K S Chouke (Endocrinology 14 169 (May-June) 1930) gave intraperitoneal injections of potassium iodide to rats and then studied the thyroid gland microscopically. In no case was the iodide found to produce a noticeable change in the character or structure of the colloid of this organ nor was there any change in the proliferative activity.

On administering potassium iodide to guinea-pigs J Rabinovitch (Am J Path 6 71 (Jan) 1930) found that the number of mitoses in the thyroid gland is high during and immediately after administration of potassium iodide but returns to normal within 3 to 7 days following cessation of the drug.

**POISONING.**—A case of fatal eruption following oral therapy with iodide is reported by J J Eller and E C. Fox (Arch Dermat and Syph 24 745 (Nov) 1931). Microscopically, peculiar inflammatory processes suggestive of neoplasm were found. Large amounts of iodide were found in the urine, skin, kidneys and liver. In this case, the patient had been using iodized salt for some years and the authors concluded that she had developed a sensitivity to such an extent that potassium iodide given in therapeutic amounts caused the fatal iododerma. They believe that the indiscriminate use of

iodized salt should be avoided and that the public should be warned of its dangers by the medical profession.

**IRIS.—ABSCCESS.**—A case of abscess of the iris in a man, aged 35, who presented an oval, yellowish-white mass in the anterior chamber, was reported by J Hansraj (Indian M Gaz 64 510 (Sept) 1929). It was mistaken for a dislocated lens, until incision was made to remove the supposed lens, when a muddy colored pus together with a little aqueous humor exuded and the mass began to disappear. It was found that the pus was coming from an opening in the iris.

W D Horner and F C Cordes (Am J Ophth 14 628 (July) 1931) report the occurrence in a diabetic patient of a metastatic abscess of the iris and ciliary body secondary to an abscess of the neck which contained staphylococci, but was almost well at the time of eye involvement. The condition began as an acute iritis and was complicated later by cataract, secondary glaucoma, and paralysis of the external rectus muscle.

**IRITIS.—Etiology.**—In order to treat iritis effectively, S R Gifford (Am J Ophth 14 100 (Feb) 1931) considers that its etiology must be determined. A careful search for *focal infection* should include examination of the tonsils, teeth, nasal sinuses, intestinal and urogenital tracts; pelvic organs, respiratory tract, gall-bladder, appendix and skin.

While many attacks of uveitis subside promptly after elimination of endogenous infections, Truman G. Schnabel (Am J Ophth 14 223 (Mar) 1931) has found that attacks may recur in spite of such treatment. Some attacks may subside without elimination of

focal infections, even when these are known to exist

Experimentally, acute and chronic iritis and iridocyclitis have been produced by a technic which shows with reasonable certainty that *focal infection* is an etiological possibility for iritis. Anemia, tuberculosis, syphilis, diabetes, lack of local tissue immunity, some selectivity on the part of the invading organism, or poor local drainage in the infected focus may be necessary for extension of focal infection to the eye.

T B Holloway (Am J Ophth 14: 232 (Mar) 1931) considers the following etiological factors in acute iritis in their order of importance: (1) Focal infections, (2) syphilis, (3) undetermined causes, (4) probable tuberculosis; (5) infectious diseases and exanthemata, and (5) skin affections.

J E Moore (Am J Ophth 14: 110 (Feb) 1931) found 249 cases of *syphilitic iritis* among over 10,000 syphilitic patients at the Johns Hopkins Hospital medical clinic. Secondary syphilis existed in 111 patients with iritis, 29 had recurrent secondary syphilis, after inadequate treatment of early syphilis; the remaining 109 cases had late syphilis. Ninety-seven per cent of the early cases, 55 per cent of the recurrent cases, and 81 per cent of the cases of late syphilitic iritis had positive blood Wassermann tests. The late type of iritis appears about 9 years after the primary infection. Iritis is more than twice as common in negroes as in whites and occurs more frequently in males of either race than in females.

So far as vision is concerned, the *prognosis* is good when early diagnosis is made and prompt treatment instituted to avoid sequelæ of iritis. Treatment of syphilitic iritis is like the treatment of general syphilis.

The clinical appearance of acute *tuberculous iritis*, rarely recognized as a distinct entity, according to William C Finnoff (Am J Ophth 14: 127 (Feb) 1931), is usually similar to acute iritis from other causes, but the former is likely to run a milder course. Acute tuberculous iritis is usually an early symptom of the chronic form of the disease in which acute relapses often occur.

**Treatment.**—According to John A Kolmer (Am J Ophth 14: 217 (Mar) 1931), there is little or no question that organisms or toxins in other parts of the body give rise to tubercular, syphilitic, and gonorrheal iritis. He advises that the general or systemic treatment of chronic recurrent iritis should be planned along the present lines of treatment of chronic arthritis, which includes a minute search for possible foci of infection. These should be removed and a careful bacteriological examination of the material made so that **autogenous vaccines** can be prepared and administered. Kolmer has obtained better results with vaccines of streptococcic and staphylococcic toxins (filtrates) than with the usual heat-killed products.

**TUMORS AND CYSTS.**—A case of *angioma* of the iris corroborated by histological examination was observed by F H Rodin (Arch Ophth 2: 679 (Dec) 1929) in a 4-year-old boy. He cites 9 other tumors reported as *angiomata* of the iris of which 3 were diagnosed by observation and 6 were found to be simple granulomata, granulation tissue, or spindle-celled sarcomata.

From a review of 25 cases of *leukosarcoma* of the iris reported in the literature, W S Duke-Elder and H. B. Stallard (Brit. J. Ophth. 14: 158 (Apr.) 1930) found that slightly more than half of the patients were males, rang-

ing in age from 1 to 80 years. The prognosis is relatively good if the tumor is completely removed either by **iridectomy**, when limited to the iris, or by **enucleation** when it has extended.

Four cases of pigmented *sarcoma* of the iris are reported by M. S. Mayou (Brit J Ophth 14:152 (Apr) 1930), who believes that the growth probably always arises from pigmented nevi. Sarcomata of the iris are rare and may be pigmented or nonpigmented. They usually occur in patients between the ages of 35 and 55. By extension of the growth into the fibers of the ligamentum pectinatum and the canal of Schlemm, increased tension results and may be the only differential diagnostic sign between a malignant and benign growth.

A *cyst* in the iris of a woman 69 years of age, which was present many months without symptoms or loss of vision was reported by Edward A. Shumway (Am J. Ophth 14:792 (Aug) 1931). Operative interference was considered unnecessary because of age, general health, and absence of symptoms.

Successful results with restoration of normal vision were obtained by R. F. Moore (Brit J Ophth 14:496 (Oct) 1930) in 2 cases of epithelial implantation *cysts* of the iris following trauma. A corneal perforation with inclusion of an eyelash in the iris had occurred in both cases. Keratitis and a woolly appearance of the iris is usually noticed at the site of the cyst.

**IRON.—ADMINISTRATION AND DOSE.**—An attempt has been made by V. E. Henderson and T. A. Sweet (Canad. M. A. J. 23:551 (Oct.) 1930) to find the most palatable form in which iron might be administered orally. They considered its combination

with tonics such as strychnine, quasia, calumba, etc. They also suggested a prescription containing sodium sulphate, which is incorporated for its laxative effect. The most palatable iron preparation which they were able to formulate was the following:

℞ *Liquoris ferri perchloridi* . . . ℥xlv (3 cc)  
*Liq potassæ* . . . ʒiij (12 cc)  
*Ammonii carbonatis* . . . gr iiss (0.15 Gm)  
*Tinctura limonis*,  
*Sp myristicæ* āā ℥viij (0.4 cc)  
*Syrupi* . . . ʒiij (12 cc)  
*Aquæ* . . . ad ʒj (30 cc)

This preparation contains approximately 5½ minims (0.33 cc) of ferric chloride solution per teaspoonful. Arsenicals, bromides and sodium sulphate may be added if desired, but strychnine in any form is not compatible. This formula must be mixed in a certain order, *viz*, the ferric chloride and syrup should first be mixed together, then the caustic potash dissolved in 15 cc (½ ounce) of water, and next the ammonium carbonate should be added, stirring well. As soon as the mixture darkens and all precipitates disappear, the other ingredients are added. Should it be desired to change the flavor of the mixture, this is easily done by simply varying the relative amounts of the several flavoring ingredients.

**PHYSIOLOGICAL ACTION.**—In experimenting with iron therapy, C. J. Polson (Quart J. Med 23:77 (Oct) 1929) found that iron was stored principally in the liver, and in smaller amounts in the spleen and lymphatic glands. Storage in the liver was much faster after subcutaneous than after oral administration, but the intravenous administration of iron caused liver storage in greater quantities than either of the other methods. Polson

also found that there was a larger amount of iron in the spleen after intravenous than after oral or subcutaneous administration and felt that this was due to a transfer of the iron from the lungs to the spleen. A small excess of iron found in the kidneys and cecum was thought to be concerned in its excretion. In no case were the lungs found to play any part in the metabolism of the iron.

V Menkin (from the Henry Phipps Institute, University of Pennsylvania) studied the effect of iron therapy on inflammatory tissue and found that in all acute inflammatory conditions in which iron therapy was being used, a high percentage of the iron could be found concentrated in the inflamed areas. This was thought to be due to an increase in capillary permeability with inflammation and fixation by the inflammatory reaction.

**THERAPEUTICS.**—N. M. Nikolajew and L. Sparo (*Zeit. ges. exper. Med.* 76: 673 (May 16) 1931) feel that the mechanism of iron therapy is not clearly understood. In a review of the literature on the subject, they found that some believe that iron absorbed by the intestine is utilized in hemoglobin formation, while others consider that iron preparations stimulate the hematopoietic system, and still a third group hold that medicinal iron serves only as a protection against loss of the iron ingested with the food. The authors studied the action in guinea-pigs and found that iron administered orally was stored mostly in the reticulo-endothelial cells of the gastrointestinal tract and in the spleen. In those cases where the medication was prolonged for over a month at a time, the iron was also found in other portions of the reticulo-endothelial system and in the epithelial cells of the

uriferous tubules. They found that the absorption and elimination of iron was extremely slow and that the different iron preparations showed a difference in their mechanical actions. A colloidal iron preparation, for instance, did not accelerate blood regeneration in guinea-pigs and no iron deposits were found in the gastrointestinal tract. On the other hand, metallic iron compounds did accelerate blood regeneration and it is believed that this form of iron should be used in the **hemolytic anemias of intestinal origin, in secondary anemias in infancy, and in those forms of anemia in which there is some disturbance of the synthesis of hemoglobin but in which erythrocyte production is normal.** Metallic iron was found to be especially helpful in the anemias of nurslings, since in these cases it reduces the absorption of toxins and also the disintegration of erythrocytes by blockade of the reticulo-endothelial system of the gastrointestinal tract.

In a discussion of the administration of iron, S. R. Mettier and G. R. Minot (*Am. J. M. Sc.* (Jan.) 1931) report 10 cases of **secondary anemia** from defective diet or chronic blood loss which were materially aided by iron therapy. In this series, the iron was administered in 3 ways: (1) in small doses with an alkaline beefsteak meal, (2) in small doses with an acid beefsteak meal, and (3) in massive doses of iron alone. The meat in these cases had no effect on blood formation but was used to help maintain the pH of the upper gastrointestinal contents approximately constant. The bone-marrow showed slightly less response in the first case than in the second and it was concluded that iron is more potent for blood formation when absorbed from an acid medium. The response of the bone-marrow to the

third type, *i e*, to doses 4 to 12 times that given in the first 2 instances, was good, which emphasizes the importance of giving iron in adequate doses rather than in continuous small doses

C G Grulee and H N Sanford (Am J Dis Child 41 53 (Jan) 1931) report the use of iron compounds injected intraperitoneally in doses of 5 mg ( $\frac{1}{12}$  grain) twice a week, combined with ultraviolet light irradiation or with whole blood transfusions. This treatment was used in children suffering from secondary anemia. In their series of cases, Grulee and Sanford found that hemoglobin rise could not be looked for in less than 30 days, but fol-

lowing that period it was increased to the extent of about 5 per cent per week. They feel that secondary anemia is due more particularly to an inability to use the iron taken into the body, rather than to an actual shortage, and that iron administered in this manner is stored up and used later. The ultraviolet irradiation seemed to favor assimilation of the iron. It was found, by associating control experiments with their clinical investigations, that iron therapy must be combined with blood transfusions or irradiation to obtain optimum results. In no case was this treatment successful in primary anemia, thus emphasizing the slight value of iron in such conditions

## J

**JAMAICA GINGER PARALYSIS.**—This disease, which is also known as “jake” paralysis and ginger paralysis, is a polyneuritis of the peripheral nerves, especially of the lower extremities but also affecting the arms and hands. When occurring in the latter, the symptoms appear from 1 to 2 weeks after the paralysis in the lower extremities.

**ETIOLOGY AND PATHOGENESIS.**—The disease is contracted by drinking impure Jamaica ginger extract, either for medicinal purposes in the treatment of acute respiratory symptoms and as a tonic during convalescence, or for the alcohol content of the extract. It is characterized by paralysis of the extremities, particularly of the legs below the knees, the extensor muscles being more affected than the flexors. This peculiar type of paralysis occurred in widely separated parts of the United States during the latter part of 1930 and the early months of 1931. The first

reports came from Tennessee where many cases occurred in the outlying districts among men who had been using Jamaica ginger extract as a beverage purely for the alcoholic content. It has been estimated that there were between 1500 and 2000 cases of this disease in the State of Oklahoma alone, according to D. T. Bowden, L. A. Turley and H. A. Shoemaker (Am J Pub Health 20 1179 (Nov) 1930).

M. I. Smith and E. Elvove (Pub Health Rep 46 1227 (May 22) 1931) studied 125 cases which occurred in Southern California during the latter part of January and the first 2 weeks of February, 1931. These cases showed the same symptoms and ran the same course as Jamaica ginger paralysis cases in other parts of the country. The authors came to the conclusion that only the early recognition of the cause and withdrawal of the extract from public sale prevented a far more serious epidemic.



When the condition first made its appearance in California, an attempt was made by the authorities to buy up all the Jamaica ginger extract available, to be used in the study of the disease, but as soon as the companies selling the extract realized that this was being done, they withdrew their stocks from sale and destroyed them. Very little aid was given the investigators in their attempt to trace the epidemic to its source and chemical and experimental research was slowed up considerably.

R. H. Goodale and M. B. Humphreys (J. A. M. A. 96:14 (Jan. 3) 1931) studied 63 cases which were brought into the Worcester City Hospital for treatment and reported the autopsy findings on 3 cases. In each of these 3 cases death could not be attributed to Jamaica ginger poisoning itself, but was caused by some complicating factor. It was significant that in all sections of the country, the Jamaica ginger extract used by patients who developed the paralysis had been shipped from New York City.

A great deal of chemical research was done by the United States Public Health Service in an attempt to determine the poisonous principle in Jamaica ginger extract. At first it was thought to be the alcohol which was used as a solvent, but this was later disproved. The theory that it might be Jamaica ginger, itself, was also excluded after careful tests, and the Public Health Service was finally convinced that the poisonous element was the triorthocresyl-phosphate which had been used by some unprincipled manufacturer as a diluent in the manufacture of the extract. In the United States Public Health News G-54, December 31, 1930, it is stated that this has apparently been substituted because of its cheapness and similarity

to ginger. It is also stated that it would take an extremely well-informed chemist to be able to differentiate this synthetic product from the real Jamaica ginger extract. In all samples obtainable, triorthocresyl-phosphate was found to be present in a 2 per cent concentration. As little as 2 Gm. (30 grains) of the chemical can produce paralysis, although experiments show that the lethal dose in man is 1 Gm. (15 grains) per kilo. (2 $\frac{1}{2}$  pounds). This would easily explain why so many cases were reported in which the ingestion of only 3 to 4 two-ounce bottles (180 to 240 cc.) of Jamaica ginger extract for medicinal purposes has been sufficient to cause the appearance of the paralysis. Triorthocresyl-phosphate is used quite extensively by chemical manufacturers as a diluent and solvent for varnishes, shellac, etc. (M. I. Smith, E. Elvove and W. H. Frazier: Pub. Health Rep. 45:2509 (Oct. 17) 1930, Reprint No. 1419).

Experimental work with triorthocresyl-phosphate when used on chickens shows karyolysis, karyorhexis and degeneration of nerve cell bodies, according to Bowden, Turley and Shoemaker (*loc. cit.*). Other experiments have shown that the monkey is not susceptible to the drug, whereas calves react to the chemical very much the same as do humans; also, it is conclusively proven that only the phosphoric acid ester of orthocresol, unlike the various other cresol esters, is capable of producing a specific paralysis of the motor nerves of the extremities in certain laboratory animals very similar to that seen in the paralysis resulting from Jamaica ginger ingestion. Studies are still being conducted with trimetacresyl-phosphate in an attempt to ascertain whether or not this ester also will pro-

duce these results, but as yet sufficient progress has not been made with the work to warrant publication (U. S. Public Health Reprint No 1419)

**PATHOLOGY.**—The relative number of deaths occurring from uncomplicated Jamaica ginger paralysis is so small that the pathology is still a mooted question. In a series of autopsies reported by Goodale and Humphreys (*loc cit*), practically nothing could be found on gross examination other than some wasting of the extensor muscles of the lower legs and of the smaller extensor muscles in the back of the hands. Microscopic examination of the spinal cord, however, showed universal migration of the nuclei to the periphery of the cells, with absence of nuclei in many cells, and fine granules in the cytoplasm of the spinal cord and anterior horn cells. The peripheral nerves showed degeneration of the myelin sheath and of the axis cylinders.

A. R. Vonderahe (Arch Neurol and Psychiat 25:29 (Jan) 1931) observed that the fiber tracts of the brain stem were untouched but there was marked chromatolysis and death of the cells in the peripheral nerves. There were also degenerative changes with loss of the myelin in the anterior roots, but the posterior roots were normal. The entire brain stem and the peripheral nerves showed considerable infiltration with amyloid bodies. The vagus nerve and other cranial nerves showed the same findings as the peripheral nerves, *viz.*, chromatolysis and death of the cells with amyloid infiltration. Vonderahe states that death was due to bulbar paralysis and his findings were substantiated by Goodale and Humphreys (*loc cit.*) In both series of cases, however, the deaths were complicated by intercurrent infections and

in only 1 instance, a case reported at length by Vonderahe, could death be truly attributed to the effect of the poisonous Jamaica ginger extract on the central nervous system.

The usual history in this disease is that a patient had been taking Jamaica ginger to clear up an acute upper respiratory infection, or attempted to obtain the alcoholic stimulation that it produced, and 1 to 18 or 20 days later had noticed slight pain first in the calves of the legs and feet, followed by numbness and swelling of the lower legs and feet. From 1 to 10 days after the appearance of the first symptoms, the patient becomes aware of the fact that he has developed foot-drop and a loss of sense of position of the limbs. Shortly after this, in many cases, weakness is noted in the hand grip, usually not preceded by the soreness that is seen in the lower extremities, with wrist-drop and a marked weakness in flexion of the fingers and adduction of the thumbs. Still later, muscular atrophy is very apt to appear, especially on the back of the hand. The affected areas are often bathed in a fine film of perspiration and have a feeling of warmth to the patient. As the weakness in the extremities progresses, some of the patients become bedridden, although they are usually able to get about with the aid of crutches or canes. When they are able to walk at all, the gait is usually staggering and resembles that of a patient suffering from locomotor ataxia. Paralysis is always more marked in the extensors than in the flexor muscles and some atrophy of the affected muscles generally occurs.

Gastrointestinal symptoms are minimal, but a mild diarrhea, with nausea and vomiting, may occasionally appear with the onset of symptoms of paralysis.

S Harris, Jr (South M J. 23:375 (May) 1930) states that a few patients complained of inability to void and had to be catheterized although this was by no means a constant finding and catheterization rarely had to be repeated more than once or twice. Respiratory difficulties are seen in most cases and take the form of rapid, gasping, shallow breathing

A neurological examination of the patient shows by no means constant findings. The plantar reflexes and the Achilles reflexes are universally absent and occasionally the patellar reflexes are either diminished or absent. In some cases a defense reaction can be elicited by stimulating the plantar surfaces of the feet, and cutaneous sensory loss and loss of vibratory sense in the affected areas is neither marked nor constant, according to H. H. Merritt and M. Moore (New England J Med 203:4 (July 3) 1930). At times the pupils show fixity to light and rather frequently one pupil is somewhat larger than the other. In commenting upon the neurological findings in this disease, G. Wilson (New York State J Med 31:70 (Jan 15) 1931) states that a neurological examination without the history of ingestion of Jamaica ginger extract would very strongly lead the physician to suspect a postdiphtheritic paralysis

**COMPLICATIONS.**—The most common complications in this disease are bilateral foot-drop, bilateral wrist-drop, loss of control of both the urinary and anal sphincters, and, frequently difficult respiration. It is of interest to note that in none of the many cases of Jamaica ginger paralysis reported has the paralysis been unilateral. The sense of pain, heat and position is usually present but tends to be slightly

diminished (Wilson). Probably the most serious complication as regards permanent disability is the strong tendency toward the formation of contractures of the flexor muscles in the affected areas. As is to be expected, this is most frequently seen where atrophy of the extensor muscles has occurred and it is extremely apt to occur if the proper treatment is not instituted early and maintained over a sufficient period of time

**DIAGNOSIS.**—The diagnosis in this condition rests almost entirely upon the history of having taken extract of Jamaica ginger medicinally or, as sometimes happens in legally arid sections, for the alcohol which it contains, and upon the fact that the paralyzes, when they develop, are bilateral, rather than unilateral, and always occur in the lower extremities before they appear in the upper. Ginger paralysis, however, must be differentiated from peripheral neuritis of infectious origin and this can best be done by obtaining a history of the use of the extract. Otherwise only microscopic examination of the nerves affected can prove that it is not infectious

**Prognosis**—The prognosis in Jamaica ginger paralysis is fair for recovery over a long period of time, despite the fact that many of the nerve cells die. It has been noted that usual function returns to the hands and wrists much sooner than to the feet and legs. This can be readily understood when it is considered that the length of the nerve fibers which must regenerate is shorter in the upper extremities (Wilson), and also that rarely have the nerve changes been found in the peripheral nerves higher up than the gluteal fold (Goodale and Humphreys). Several cases have been reported in which death occurred

in these paralyzed patients, but in almost every series the paralysis has been complicated by other conditions. Goodale and Humphreys (*loc cit*) reported autopsy findings on 3 cases of ginger paralysis that were studied by them at the Worcester City Hospital but all of these were complicated by other factors and it was felt that the concomitant factor, rather than the Jamaica ginger paralysis, was the cause of death. Vonderahe reports 9 autopsies on similar cases, but only 1 death in his series could be attributed to the ginger paralysis, *per se*. Both authors agree that when death does occur, it is due to respiratory failure from bulbar paralysis.

**TREATMENT.**—The consensus of opinion in the treatment of Jamaica ginger paralysis seems to be that great stress should be laid upon the general **hygienic care** of the patient, combined with **absolute rest in bed** during the acute stage and **immobilization of the affected parts** in such position that no contractures may form because of overaction of the flexor muscles. After the acute stage has subsided, however, **gentle massage** and **galvanic electric treatment** should be tried. At this time, it is more of an orthopedic and neurological than a purely medical condition. A considerable time will be required before complete restoration of function is obtained. Goodale and Humphreys (*loc cit.*) were able to study many of their cases 6 months after discharge from the hospital and found that in most cases complete function had returned to the upper extremities but the lower extremities were still partially paralyzed, although much improved over the condition in which they left the hospital. This is to be expected, since the lower limbs are more seriously affected in the first place, and the nerve

fibers which must regenerate are so much longer.

**JAUNDICE.** See LIVER

**JOINTS.—KNEE.**—The synovial sacs of the knee and the approximo tibio-fibular joints communicate in about 15 per cent of all cases, according to Carnes Weeks (*Am J Surg* 8 798 (Apr) 1930). Where no such communication exists, the close proximity of the 2 synovial sacs necessitates injury to the popliteal bursa in exarticulation of the fibula. Acute suppurative arthritis of the knee joint may readily follow removal of the head of the fibula in the presence of infection.

**SACRO-ILIAC JOINT.**—In a review of 257 postmortem specimens in sacro-iliac joints B. David Sashin (*J Bone and Joint Surg* 12 891 (Oct) 1930) divides his material into 3 groups: (1) 1 to 29 years of age, (2) 30 to 50 years of age; (3) 60 years of age and above.

In group (1) the findings were summarized as follows: (a) The sacro-iliac articulations are true diarthrodial joints. The joint surfaces are covered with hyaline cartilage and there is a joint space, synovial membrane, synovial fluid and slight motion. Mobility was slight but present, and consisted of upward and downward, and forward and backward motion. Arthritis was not seen.

In group (2) the findings were as follows: (a) In males, mobility was present to a slight degree until the fourth decade. In females motion was present until the fifth decade. Bony ankylosis was present in 51 per cent of males and 58 per cent of females. Osteoarthritis was found in 91 per cent of males and 53 per cent of females.

In group (3) the findings were as follows: (a) Degenerate changes in the

articulate cartilage of specimens were found in all sacro-iliac joints. Bony ankylosis was found in 87 per cent of male joints and 30 per cent of female joints.

The indications for fusion according to W. C. Campbell (South M. J. 24: 186 (Mar.) 1931) are

- (a) Failure of conservative methods.
- (b) Tuberculosis of the sacro-iliac joint.
- (c) Abnormalities and destructive changes shown by x-ray and not responding to treatment.

(d) Persistent symptoms after conservative treatment even if the x-rays are negative.

The technic of the operation is described as follows. Three adult dogs were operated upon and bone grafts taken from the crest of the ileum were inserted between the ileum and the sacrum. The grafts were inspected within 3 months and excellent bone fusion was found to be present. The technic is simple, surgical risk slight, the procedure entirely extraarticular, and fusion causes no disability.

## K

**KIDNEY.—DIAGNOSTIC MEASURES.**—The differential diagnosis of acute *pyelitis*, *hydronephrosis* and symptomless *hematuria* is discussed by R. M. Handfield-Jones (Lancet 2: 1135 (Nov. 30) 1929). He states that one method of investigation of peculiar interest in renal lesions is the *hyperesthesia test of the skin* in these cases. Renal lesions give a high proportion of positive tests and the areas should always be mapped out if present. No negative hyperesthesia test is of any value but a positive one may prove to be the conclusive piece of evidence needed. He stresses the point that in every case of abdominal pain the urine should be examined and the kidneys remembered as a possible source of the trouble.

**Kidney Function Tests.**—Regarding kidney function tests, B. A. Thomas (J. Urol. 24: 2 (July) 1930) gives a very interesting discussion. For practical purposes the author states that these tests may be divided into: (a) blood biochemical tests of nitrogen retention, and (b) the kidney test of elim-

ination of endogenous (urea and chloride) and exogenous (indigo-carmin and phenolsulphonphthalein) products. The first group depends upon the determination of the nitrogen retention in the blood in the event of renal disease and are total nonprotein nitrogen, urea nitrogen, urea salivary index, creatinin, uric acid and plasma CO<sub>2</sub> combining power. The first is by far the superior one, but, because of laborious laboratory procedures, is replaced by the second as a routine test. The remaining estimations, with the exception of the creatinin, are of little value, according to Thomas.

In considering the *functional test of elimination*, the urea concentration factor has been found exceedingly sensitive, but it requires a good deal of time and trouble and, therefore, it is not nearly so popular as the dye tests. The author is particularly enthusiastic concerning the indigo-carmin and he has worked out an efficiency test which he calls the "index of elimination." This term may be defined simply as the ratio of the output of the first and third

periods of the normal cycle of elimination of the dye or other excretory product. Normally, the kidneys will eliminate several times as much dye in the first period as in the third 20-minute period following the intravenous administration of the dye. If there is a functional impairment, the onset of elimination is markedly delayed and there will be a relatively larger output in the third period than in the first. So long as the output in the first period exceeds that of the third period, the index is said to remain in the positive phase and it is safe to perform the necessary surgery. If the index is in the negative phase because the third period output is higher than the first, surgery is contraindicated. The author believes that in cases of obstruction no test of elimination can be relied upon exclusively and it is here that blood chemistry admirably fills the gap.

**Pyelography, Intravenous.\***—According to A. Viethen (Ztschr. f. Kind. 50:141 (Oct. 15) 1930), intravenous pyelography is of especial value in children in the diagnosis of malformation of the urinary tract, as a differential diagnostic aid in obscure abdominal conditions, in suspected tuberculosis of the urogenital system, in lithiasis and in chronic pyuria. It is *contraindicated* in complete inhibition of the secretion of urine and in conditions in which the functioning of the kidneys is decreased only because the secretion of iodine would occur slowly. It is also contraindicated in tuberculosis, iodine idiosyncrasy and thyrotoxicosis.

**Indications**—The indications for intravenous pyelography with uroselectan are listed by A. von Lichtenberg (Radiology 15:664 (Dec.) 1930) as follows: (1) In those cases in which cystoscopy,

catheterization of the ureter and instrumental pyelography cannot be performed because of anatomic, pathologic or technical reasons, (2) in all cases of ureteral obstruction in which the contrast substance introduced by means of instrumental pyelography does not pass the point of obstruction; (3) in those cases in which instrumental pyelography cannot be undertaken without risk to the patient. A diagnostic film is to be expected only in those cases in which renal function is present and the density of the shadow is dependent on the amount of function which exists. In severe bilateral infections of the kidneys, particularly those conditions associated with a damaged parenchyma purulent in character, this shadow will be absent, faint or considerably delayed.

**Pain in Renal Diagnosis.**—A most interesting study of the pains provoked by palpation and their interpretation by painful points in renoureteral affections has been made by E. Papin (Arch. d. mal. d. reins 4:1 (June); 253 (Oct.) 1929). He finds that a low floating kidney when grasped between the two hands provokes a peculiar painful sensation similar to pain associated with pressure on the testicle.

In renoureteral disturbances, the painful points are of 2 kinds: those situated on the course of the dorsolumbar nerves and those on the course of the ureter. The ureteral points are 3: the superior, median and inferior. The superior ureteral or paraumbilical point is situated on the abdominal wall on a horizontal line passing through the umbilicus toward the external edge of the great rectus muscle but inside it. This point is quite constant in pyelitis. The median ureteral point seems unquestionably to correspond to the ureter itself, as does the lower point.

\* See also Urography



Renal pain starting in the renal parenchyma of the pelvis is transmitted to the nerve centers by way of the renal plexus and thence is reflected to the course of the dorsolumbar nerves. In renal disease the contraction of the parietal muscles is observed and also that of the cremaster. The beneficial action of dry cupping and scarification of the lumbar region in renal diseases is explained by the reflex vasomotor stimulation of the tissues arising from the same metamere.

Spontaneous pain in renal disease as explained by the author may be continuous or occur in more or less acute attacks. Acute apyretic attacks include: (1) renal colic in lithiasis, hydronephrosis, floating kidney and tuberculosis and cancer, (2) renal strangulation due to a torsion of the pedicle, and (3) neuralgia of renal origin. The febrile acute attacks include (1) attacks of retention occurring in such conditions as pyelonephritis with distention, pyonephrosis and hydronephrosis, and (2) infectious perinephritis bordering or not on the formation of a perinephric abscess.

**HYDRONEPHROSIS.—Etiology.**—As explained by R. P. Rowlands (Brit M J 2 681 (Oct 25) 1930), this disorder is usually the result of an obstruction to the flow of the urine along the ureter. This obstruction may be the result of a stone in the ureter, a stricture or a kink of the ureteral wall, pressure from without or to a valvular condition at the upper end of the ureter. Frequently, according to the author, there is a congenital narrowing at the junction of the renal pelvis and the ureter, and sometimes there is a valvular fold at this point. Any of these conditions result in a distention of the pelvis, especially in a mobile kidney.

**Diagnosis.**—Repeated attacks of pain in the loins, both back and front are the chief complaints. The pain rarely radiates, dysuria and abnormal urine are the exception, but the attacks gradually become more severe. Eventually, a typical hydronephrotic swelling develops and occasionally pyonephrosis, with or without pathological urine. This obstruction when seen at the operating table is better treated by (1) enlarging the outlet or by (2) anastomosis between the lower pole of the renal pelvis and the ureter.

C. Gauthier and C. Clavel (J. d'urolog. 30: 371 (Oct) 1930) claim that in some cases of hydronephrosis the only manifestation is in the form of gastrointestinal symptoms, due to a reflex disturbance of the secretion of the stomach and intestine from the renal distention, compression or kinking of the intestine from sudden variations in the size of the kidney, and urinary insufficiency from gradual atrophy of the renal parenchyma. In many instances the symptoms simulate mucomembranous enterocolitis, dysentery, appendicitis, sigmoiditis or a gall-bladder condition. To the authors, indispensable aids in the diagnosis of a latent hydronephrosis are ureteral catheterization and pyelography.

**NEPHROPTOSIS.**—B. A. Thomas (J. Urol. 22: 603 (Dec) 1929) believes that many patients with nephroptosis would be spared many years of invalidism, renal destruction and even loss of life if they were properly treated. Neglect often means the occurrence of bacilluria, pyelitis, loss of renal function and destruction of the kidney. The author was led to this study as a result of the unsuccessful attempts at palliative measures with external abdominal support in an effort to relieve these

patients In his series, he found that the subjective symptoms presented are by no means an accurate measure of the mobility of the kidney and this degree can only be determined by urologic examination

**Treatment.**—Thomas (*Ibid*) states that the treatment must not only be aimed at the relief of the symptoms, but also to prevent those factors which might lead to an insidious destruction of the kidney by hydronephrosis and infection Palliative treatment is contraindicated when (1) subjective symptoms are not controlled by supportive appliances; (2) the threat of renal damage from urinary retention and infection is not controlled; (3) severe infection, calculus or tumor formation of the kidney is present; (4) there is a rotation of the kidney and a kink in the ureter, and (5) the kidney is movable to more than the first degree The author believes that surgical intervention has much to offer and the incidence of failure should not be more than 10 per cent.

A series of 65 cases of ptosis of the kidneys were treated by Munz, Abud and Liva (*Rev méd. de Chile*, 58:845, 1930), 35 being treated surgically and in the other 30 the nonsurgical treatment was given because of refusal of surgery or serious insufficiency was present. Of the 35 which were operated, 18 complained and were suffering from a chronic appendicitis In 50 of the 65, there was an evidence of marked enteroptosis

According to the authors, the presence of chronic appendicitis may be masked by reflex pain, but often there is a pain medial to the anterosuperior spine of the ilium This point was lateral to and below McBurney's point. The authors having considered the marked association of the 2 conditions,

are routinely performing an appendectomy in all instances where they open the abdomen for a nephroptosis

#### PERINEPHRIC ABSCESS.—

**Diagnosis.**—An analysis of the records of 55 cases of perinephric abscess has been made by H C Rolnick and H J Burstein (*J Urol* 25 507 (May) 1931) in which the most valuable diagnostic aid was puncture and aspiration This procedure has been bitterly condemned by many observers but the authors point out that the objections are usually theoretical Most authorities are of the opinion that metastatic abscesses are secondary to an extension from metastatic infarcts of the kidney to the perinephric tissue Of the 12 cases which the authors punctured, 8 were positive for abscess In 1 case which was negative, there was a large amount of pus at the operation and in another negative case it was proven that pus was present by cystoscopy and in another by surgery

#### RENAL COLIC.—*Etiology.*—

W E Wilson (*Brit M J* 2:101 (July 18) 1931) reports on an incidence of renal colic following recumbency He was serving in the specialized hospitals of Great Britain during the Great War and observed that in the femur wards about 15 per cent of the patients developed renal colic when the actual pain was probably due to the passage down the ureter of large quantities of blood This was seen particularly when the men assumed an upright position after long decubitus The symptoms disappeared in within 2 or 3 days and in only 1 instance was there an actual calculus formation He attributes the upright position as the cause of the hematuria and believes that if the men had not been so anxious to show what they were capable of doing on their feet,

there would be fewer cases of renal colic

**TUBERCULOSIS.**—According to J R Caulk (J Urol 26 189 (Aug) 1931), renal tuberculosis is declining in frequency as a result of the improvement in the early diagnosis and treatment of pulmonary and general tuberculosis and the prevention of massive lesions. When an infection of the bladder has occurred the cystoscopic examination is quite characteristic, according to the author.

**Etiology.**—H C Bumpus and G J Thompson (Am J Surg 9 545 (Sept) 1930) refute the old idea that renal tuberculosis is always secondary to a pulmonary lesion. They point out from their large series of cases that it may occur coincidentally with tuberculosis of other parts or organs of the body. They conclude that the initial lesions of the kidney frequently heal, that it is impossible for a normal kidney to filter bacilli of tuberculosis out of the stream, that the presence of the tubercle bacilli always means renal involvement, and that the dysuria is a symptom of urinary tuberculosis and does not occur in tuberculosis confined to the genital tract.

**Diagnosis.**—J Martin (J d'urol 29. 556 (June) 1930) discusses the difficulties and errors involved in the diagnosis of renal tuberculosis, especially in those cases in which some of the indications may be lacking. He finds that a pyuric kidney, in the urine of which tubercle bacilli have been found, is not necessarily tuberculous, neither is a decided deficiency of urea concentration on one side necessarily an indication of tuberculosis of that kidney. Thus, unless tubercle bacilli are actually found in the urine originating from the kidney, further examination should be made.

**Treatment.**—In unilateral renal tuberculosis, **nephrectomy** should be performed promptly, but surgery in bilateral lesions is indicated only in case of an emergency to relieve toxemia from pyonephrosis or to correct intractable vesical lesions, according to Caulk (*loc cit*). He believes the chance of healing in chronic renal surgical tuberculosis is remote and not comparable with the simple early experimental lesions. The mortality of nephrectomy is exceedingly low and the relief of the bladder symptoms may be expected in at least 75 per cent of the cases of unilateral disease.

**TUBERCULOSIS IN CHILDREN.**—A comprehensive bibliographic review of the subject of renal tuberculosis by A Bekkerman (J. d'urol 31 236 (Mar) 1931) concludes as follows. The laws which govern the conditions associated with renal tuberculosis are the same for children as for adults. Renal tuberculosis in children is not frequent. The mortality is inversely proportional to the age. In the majority of cases the primary focus of the infection is discovered. Each time that an anomaly is observed in the child's renal system, it is indispensable to proceed with a complete urologic examination without taking into consideration the patient's age, and utilizing all adequate instrumentation. Lack of technic and absence of necessary apparatus, as well as certain peculiarities in the disease, hinder certain measures being carried out that would increase the possibility of an early diagnosis. The treatment of juvenile tuberculosis is similar to that for adults. In a number of patients with pulmonary tuberculosis cared for at the dispensaries, those disorders must be associated with urogenital tuberculosis.

## L

**LACRIMAL APPARATUS.**

—**LACRIMAL GLANDS.**—*Tuberculosis.*—A case of tuberculous dacryoadenitis was observed by M P Motto and E H Rowen (Am J Ophth 12 818 (Oct) 1929) in an 8-year-old colored boy who had tuberculosis of the spine. He developed a fluctuating swelling on the left upper eyelid. Histological examination revealed lacrimal gland tissue which showed tuberculosis.

*Tumors.*—W L Benedict and A. C Broders (*Ibid* 13 585 (July) 1930) stress the situation of the lesion in the superior temporal region, the time of life at which it appears, and the development of exophthalmos as important points in making a diagnosis of *adenocarcinoma* of the lacrimal gland.

**LACRIMAL SAC AND DUCT.**

—F. H. Diggle (Brit M J 1:391 (Mar. 7) 1931) reports that 73 per cent of the patients in whom *intranasal dacryocystorhinostomy* for the relief of *lacrimal obstruction* was performed were completely cured. They were free from epiphora even when out of doors.

Operative intervention in *dacryocystitis* and *dacryostenosis*, is believed by E. Kuklefeldt (Finska lak-sällsk. handl 72. 425 (June) 1930) to be rarely necessary, even in very grave cases. In his experience conservative treatment has always given good results.

For lacrimal sac surgery, D B Kirby (Am J. Ophth. 14 672 (July) 1931) has devised a blood-suction cannula similar to that used by nasal surgeons for the removal of blood from the operative field.

**LARYNX. — HOARSENESS.**

*Differential Diagnosis.*—The differential diagnosis of hoarseness is most

important from the standpoint of prognosis, since grave consequences result to the individual when the condition remains unrecognized during the time when curative procedures can be resorted to. The various causes of hoarseness have been well described by J E Mackenty (Arch Otolaryn 9 237 (Mar) 1929).

1. *Simple chronic inflammations* Secondary to chronic nasopharyngitis, infected teeth, chemical irritants, tobacco, alcohol, etc

2. *Specific chronic laryngitis* Syphilis, tuberculosis, rhinoscleroma, leprosy

3. *Neoplasms* Papilloma, angioma, fibroma, singers' nodes, carcinoma

4. *Paralyses*

5. *Prolapse of the ventricle* of the larynx.

The most important conditions as enumerated above which require differential diagnosis are syphilis, tuberculosis and cancer. *Secondary syphilis*, as a rule, is a diffuse infection and luetic patches may spread over large areas. The Wassermann reaction is positive. In *tertiary syphilis* the gummatous lesion may occur in any part of the larynx. There is marked redness over the infiltrated area, as well as in the surrounding mucous membrane. When there is breaking down the resultant ulceration is deep with sharp edges. Pain is usually absent and fixation of a cord is a late manifestation.

The predilection sites for *tuberculosis* are: (1) interarytenoid area and arytenoid; (2) vocal cords; (3) false cords, (4) epiglottis. The involvement is usually bilateral, the areas are rather pale in contrast to lues, which are markedly injected. Ulceration occurs

early, as well as pain and dysphagia. The cords, as a rule, remain movable. Smears show tubercle bacilli.

**Early cancer** of the larynx is unilateral. It usually begins in the middle-third of one vocal cord, the pain and ulceration are later manifestations but fixation of the cord begins early. When the carcinoma has involved the lymph gland or has extended beyond the confines of the glottis, the case is, as a rule, hopeless. Although cancer of the larynx is usually present in people of middle age it does occur in young adults. J. E. Mackenty (*Ibid* 10: 585 (Dec) 1929) reports a case of intrinsic basal cell epithelioma of the larynx in a young woman, age 20, whom he treated by total laryngectomy.

The physician must not be misled in the diagnosis of malignancy by the presence of another condition such as tuberculosis or syphilis, for many cases have been reported in whom all 3 conditions were present at the same time.

**X-ray Diagnosis.**—While not an entirely new subject, it has received impetus through an excellent paper by G. T. Pack and L. F. Craver (*Ibid* 13: 658 (May) 1931), who advise lateral x-rays of the neck as useful supplementary means of studying tumors about the larynx and thyroid. These studies are useful in such conditions as tuberculosis, syphilis and carcinoma of the larynx, tracheal stenosis, carcinoma of the thyroid, retropharyngeal tumors and neoplasms at base of tongue. H. K. Pancoast (*J. A. M. A.* 95: 1318 (Nov. 1) 1930) also emphasizes the need for x-ray study of the upper respiratory tract in the neck, both fluoroscopic and x-ray technic being essential.

An interesting case is reported by G. Tucker (*Ibid* 96: 1572 (May 9) 1931) in a woman 57 years of age who was

hoarse for 6 weeks. Biopsy revealed both tuberculosis and cancer in the same lesion. While such an occurrence is unusual, it must not be regarded as rare, and in some instances a + plus Wassermann may not be amiss.

**PSEUDVOICE PRODUCTION.**—Morrison (*Arch. Otolaryng.* 14: 413 (Oct.) 1931) calls attention to the fact that with the increasing number of persons rendered voiceless by total laryngectomy for laryngeal cancer, there is a growing need for a therapy of pseudovoice production without the larynx. Patients with a complete, chronic, air-tight stenosis of the larynx from any cause are similarly in need of a pseudovoice. Laryngeal prostheses, or artificial larynges, have so many disadvantages that their use should be restricted to the patient who cannot learn to produce any type of pseudovoice. There are several types of mechanism of the production of a pseudovoice. One is the true buccal or pseudowhispered voice. Almost every laryngectomized patient learns it without difficulty; it is so faulty and imperfect that it should be employed only when a more satisfactory type cannot be produced. The pharyngeal pseudovoice is usually fairly satisfactory. It is produced with the aid of a pseudoglottis formed at the back of the mouth or in the hypopharynx, where air that has been aspirated or swallowed into a vicarious air chamber in the lowest hypopharynx or the esophagus and expelled again is set into audible vibrations; such sounds are modified into the vowels and consonants of the pseudovoice. One of the most perfect forms of the pseudovoice is the esophageal type, in which the vicarious glottis lies at the esophageal mouth of Killian, and the vicarious air chamber is formed within the lumen of the esoph-

agus, particularly in its cervical and upper thoracic portions. Here the mechanism of pseudovoice production is strikingly like that of normal speech. In some cases the cardiac end of the stomach, with the stomach air bubble, may be the vicarious air chamber, which furnishes a stream of air for a pseudoglottis at one of the sites mentioned.

A fairly definite system of therapy directed toward teaching the patient to produce one or another of the types of pseudovoice has been elaborated. It seems essential that all surgeons who perform total laryngectomy or who have patients with complete, chronic laryngeal stenosis should be aware of the facts given and should attempt to aid these voiceless persons in securing a useful pseudovoice, such patients will not be cut off in their social intercourse, nor will they be unable to earn a living because of their lack of intelligible speech. Having in view the fact that almost all laryngectomized patients can learn a pseudovoice, the laryngeal surgeon should, if it is possible, so conduct the operation as to favor the production of the pseudovoice, at least, on anatomic and physiologic grounds.

#### LARYNGEAL TUBERCULOSIS.

—H. Schugt (Munch med Wchnschr 77 626 (Apr 11) 1930) describes his observations on patients with tuberculosis of the larynx who were treated according to Leichsenring's method. In order to secure rest for the diseased larynx, the recurrent nerve is temporarily paralyzed. The exclusion of the nerve is done either by injection of alcohol, as advised by Leichsenring, or by surgical intervention. The author employed the first procedure, because it is simpler and less dangerous than surgical division. He uses an 85 per cent alcohol solution to which several drops

of a 1 per cent solution of procaine hydrochloride are added. The injection needle is from 8 to 10 cm long. The point of puncture between the cricoid cartilage and the first tracheal ring is marked on the skin. The needle is pushed through up to the spinal column, then it is retracted from 1 to 1.5 cm and the alcohol is injected.

The author employed this treatment in 25 cases. In some instances the paralysis developed immediately, in others the injection had to be repeated. Because the vocal folds frequently remain in the median position following the exclusion of the nerve, a bilateral paralysis is not advisable on account of the danger of suffocation and because of a possible disturbance of the mechanism of coughing. In case of unilateral paralysis, these dangers are avoided. The rest that is secured for the diseased larynx by the exclusion of the nerve is more complete and more effective than refraining from speaking. The average duration of an effective paralysis is from 4 to 8 weeks.

A factor that speaks against the surgical exclusion of the nerve is that sometimes the vocal folds do not return to the normal function. Occasionally this occurs also in case of alcohol injection. The author believes that this might be avoided by using a weaker solution of alcohol. If the paralysis is only unilateral, the patient's voice is not impaired, even if on the one side the nerve is not restored to the normal function, because the other vocal fold becomes adapted.

In 15 of the 25 patients treated with this method, the observations are complete: 9 of the patients recovered, 3 showed no improvement, in 2 the disease progressed, and information could not be obtained about one case. The



other 10 patients are still under observation. On the basis of his experience the author concludes that Leichsenning's method for exclusion of the nerve can yet be improved. He asserts that it is not dangerous and gives good results. Therefore, he recommends its application.

F Heaf (Tubercle 12 241 (Mar) 1931) states that all patients with tuberculous laryngitis, except those that are hopeless, should be advised to try to **keep silent**, and they should be provided with a pencil and a notebook to write down all their conversation. Whispering is not recommended, as it causes considerable laryngeal movement. It is best to instruct the patient to keep absolute silence, and then allow him to use his voice normally for 1 hour each day, increasing the period by hourly increments every 3 or 4 days if the larynx remains quiescent. It is also particularly desirable that useless coughing should be checked as much as possible during treatment. The advice to keep silent is difficult to follow, and it is rare to find a patient who is conscientious in this direction, particularly among the poorer classes. It is, therefore, necessary to assist the patient with further treatments. These may be classified under the following headings: **local applications** (respirators, insufflations, painting with caustics), **cauterization**, **heliotherapy**, **external applications** (blisters), **injection of superior laryngeal nerve**, and **surgical methods**. It must be remembered, however, that **silence** and the **galvanocautery** are the 2 most important and effective methods of treatment.

**PERMANENT TRACHEOTOMY.**—At the Section of Laryngology of the Royal Society of Medicine, Sir St. Clair C. Thomson read an important

paper on permanent tracheostomy in **stenosis of the larynx** and showed a series of cases in which it had been successful (J A M A 97 472 (Aug 15) 1931). The stenosis was due to various causes—*malignant disease, trauma, bilateral laryngeal paralysis, tuberculosis, syphilis, lupus* and *laryngofissure*, which was repeated for recurrence of growth. A study of tracheotomy had impressed him with some paradoxes. It was usually done reluctantly, often it was delayed until it was difficult and even useless to do, and sometimes it was imperfectly done. Also, the cannula was often taken out too soon. Most cases of stenosis were due to a *badly performed tracheotomy*, and the first step to correct a stricture was often a proper tracheotomy performed at the right level. Bronchitis was commonly held to be a direct result of wearing the tube and inspiring cold air through it, but this was not Thomson's experience, none of his patients suffered from it. The tube orifice could be concealed behind the neck wear, and removal for inspection and cleaning was necessary only every 3 months. With the speaking valve attachment the voice was easily produced and was often normal. One woman, now aged 87, had worn the tube for 70 years and never had bronchitis. The common mistake was to divide the first ring of the trachea or even the cricoid, thus introducing the cannula into the narrower and sensitive subglottic region.

In the discussion, the other laryngologists endorsed Sir St. Clair Thomson's views, but Professor Portmann, of Bordeaux, stated that he had found many men with stenosis following *war wounds*. He did tracheostomy and cleared away the cicatricial tissue. After the stenotic process had ceased he did a **plastic operation**, which he thought

was preferable to the patient always wearing a tube

**CHRONIC STRIDOR IN CHILDHOOD.**—*Diagnosis.*—According to R L J Kennedy and G B New (J A M A 96 1286 (Apr 18) 1931), the diagnosis of enlarged thymus is frequently made in cases in which further examination has disclosed other conditions as the cause of symptoms. Stridor, dyspnea, hoarseness, spells of cyanosis and wheezy and noisy respiration can usually be accounted for on other bases than that of enlarged thymus.

*Laryngoscopic examination* is frequently essential for definite diagnosis. Enlargement of the thymus can seldom, if ever, be established as a cause of death. Preoperative examination and care of infants and children should be directed toward finding and correcting all conditions affecting surgical risk. Unwarranted publicity has been accorded the assumption that enlargement of the thymus accounts for much morbidity and mortality in infancy and childhood. In the author's experience it has been unnecessary to carry out preoperative x-ray treatment of the thymus.

**LEAD.—PHYSIOLOGICAL ACTION.**—In studying the action of lead, R A Kehoe and F Thamann Miyasaki (Arch f. exper Path u Pharmacol 150.39 (Apr) 1930) found that absorption of the lead is delayed when a solution of dialyzed iron or milk is given at the same time. He explains this as probably due to the formation of a colloidal lead phosphate from the phosphatic content of the milk.

On experimenting with tetra-ethyl lead R A Kehoe and F. Thamann (Am J. Hyg 13:478 (Mar) 1931) observed that it was absorbed through

the skin in many cases, but that it is so rapidly decomposed by the tissues that only a small portion of the lead found later in the blood is in the form of tetra-ethyl lead. In all cases, within a few days the lead in the animal tissue was distributed in a manner characteristic of water soluble compounds and was excreted from the body as such. They found that any amount of tetra-ethyl lead absorbed from *gasoline* in concentrations of less than 0.1 per cent. could be disregarded, an observation of considerable practical importance.

Studying the action of lead on long bones, E. C Vogt (Am J Roentgenol 24:550 (Nov) 1930) noted that it was deposited in unusually dense zones at the ends of the diaphyses in the rapidly growing areas. This could be demonstrated by x-rays. Vogt's findings were substantiated by J Caffey (Radiology 17:957 (Nov) 1931), who reported 3 cases of chronic lead poisoning in children, and by E A. Park, D Jackson and L Kajdi (Am J. Dis Child 41 485 (Mar) 1931), who also reported a series of cases.

An attempt has been made by M D Devlet-Kildeeva and B A Raikhshtein (Kazansky M J. 26 690 (July) 1930) to determine the action of lead on the uterine musculature. They found that with very dilute concentrations of lead acetate, hypotonia of the uterus and weakness and slowing of the muscular contractions were present. When the concentration was increased, the muscular contractions became stronger and more frequent and the uterus became more hypertonic. When the concentration was increased still more, the uterus reached a complete tetanic condition and even after all acetate solution had been washed away, the uterus could not be relaxed again.

In commenting on the rôle of lead in visual disturbances, F G Pedley (*J Indust Hyg* 12 359 (Dec) 1930) states that there were only 4 cases of *eye involvement* in 100 cases of plumbism. In none of these could the visual pathology be definitely attributed to the action of the lead compounds on the optic nerves.

After observing the excretion of lead following injection, R K Newman (*M J Australia* 1 781 (June 14) 1930) believes that the therapeutic action is a quantitative rather than a qualitative one. He studied the excretion of lead in the urine and in the feces and found that it would take approximately 10 weeks for the complete excretion of a single injection of 50 mgm ( $\frac{5}{8}$  grain) of lead. Under these circumstances lead therapy would be quite dangerous if given in sufficient doses, but without effect if given in doses that could be excreted.

**POISONING.**—During the past 2 years a great deal has been written concerning the use of lead as a therapeutic agent and the possible sources of lead poisoning. H Hegna (*Norsk mag f laegevidensk* 91:673 (June) 1930) reports a series of 6 cases of lead poisoning due to the *inhalation of lead dust* by men at work. R. F Reitzel (*Ann Int Med* 3:378 (Oct) 1929) reports a series of 4 cases of lead poisoning occurring through the use of snuff. This was thought to be due to one of 3 causes, *viz*, (1) an adulteration in manufacture; (2) the fact that the wrappers may contain lead, and (3) that the spray used as an insecticide in the cultivation of the plant not infrequently contains lead arsenate. These cases of lead poisoning were usually seen where snuff in large quantities had been used over a long period of time and in most

cases the symptoms cleared up soon after the habit was stopped.

The importance of the mild lead poisoning which is fairly common among children in Queensland, Australia, is commented upon by S F McDonald (*M J Australia* 1 806 (June 21) 1930). He feels that blood examination and examination of the urine for lead are not final diagnostic points, but that the most important factor is the finding of a supply of available *lead paint*.

U S Public Health News H-9 (released February 20, 1931) comments on the possibility of children contracting lead poisoning through nibbling at the *paint* on their cribs and toys, and warns manufacturers to use only those paints which do not contain lead. Similarly, they warn parents of all children who may show such perverted appetites, when repainting, to use enamel, quick drying lacquers, etc., rather than leaded paints.

In a monograph on plumbism, N Porritt (*Brit M. J* 2:92 (July 18) 1931) divided his cases into 2 types, one, the classic form of lead poisoning, acute in action and caused by massive doses, and the other a slow, insidious, subtle condition, due to long continued ingestion of very small amounts of lead. In commenting on the second class, Porritt relates his experience with several cases in which there was extreme lethargy with a "weariness of flesh and brain" and loss of interest in the surroundings. The general appearance might be good, the appetite and sleep normal and the blood changes slight. In some cases the patient was the only person in the household to act so strangely, since lead has a selective action, and was considered by the rest of the family to be morose and uncon-

genial and received little sympathy. Lead usually could be detected in the urine and in the *water* that these people had been drinking over a period of years. In most cases, the water came from boggy moorlands and peaty marshes. The water was soft in character and absorbed the lead, while being piped through lead pipes, in sufficient concentration to cause the trouble. When these patients were sent away, or the water supply was changed, their general health and morale immediately improved.

E Bramwell (Brit M J 2:87 (July 18) 1931) corroborates the findings of Porritt to a great extent except that, in those cases who do not show lead in the urine and where an obvious source of lead cannot be detected, he believes lead poisoning can only be diagnosed after a careful consideration of the clinical picture and of the possible sources of supply. These authors agree that diagnosis is materially aided by sending the patient to a new environment for a period of time (since lead is soon excreted and, with excretion, the symptoms disappear) and by watching for a recurrence upon return to the old environment.

Three cases showing the clinical signs of lead poisoning are reported by M Nedok (Wien klin Wchnschr. 43: 427 (Apr 3) 1930) in which the diagnosis was clinched by finding reduced hemoglobin content and granular basophilic degeneration of the erythrocytes. The source of the lead in these cases was new wine which had been drained from the presses through *lead pipes*. The symptoms cleared up when further use of the wine was stopped.

In a study of the toxicity of various lead compounds J. S. Buck and D. M. Kumro (J Pharmacol. and Exper

Therap 38 161 (Feb) 1930) found that tetra-methyl lead showed a relatively low toxicity when compared with the other lead compounds. These investigators attempted to use this tetra-methyl lead compound in the treatment of tumors but as yet no marked success has been obtained.

**THERAPEUTICS.**—L. C. Knox (Am J Roentgenol 23:304 (Mar) 1930) reports 70 cases of **cancer** treated with *colloidal lead* and believes that in some cases the lives of the patients have been prolonged and an occasional permanent cure has been obtained. She feels, however, that it is most satisfactory in young patients who are not anemic or cachectic, and who do not have extensive metastases. She believes that x-ray treatment at the same time makes the lead treatment more efficient. F. C. Wood (Am J Roentgenol 23 299 (Mar) 1930) corroborates the statements of Knox.

**LIPIODOL.**—E. Erdesz (Munchen med. Wchnschr 77 439 (Mar 14) 1930) reports a case in which low-grade spondylitis and myelitis was definitely improved following x-ray examination in which iodized sesame oil was used as a contrast medium. It was thought that the result was due to iodine freed from the solution.

T. H. Amako (Zeit f Tuberk 58 178 (Oct) 1930) used iodized sesame oil in the hope that it would have a bactericidal action but concluded that too much reliance should not be placed upon it.

**ADMINISTRATION.**—W. B. Wood (Lancet 1 1339 (June 21) 1930), in discussing the administration of iodized oil, believes that oral injection should be satisfactory in the differential diagnosis between upper lobe

*bronchiectasis* and *pulmonary tuberculosis*

**UNTOWARD EFFECTS.**—R B Bettman, J Kelly and N Crohn (Arch Surg 19 471 (Sept) 1929) report the use of iodized poppy seed oil in experiments on dogs. Intrabronchial injection was not followed in any instance by pneumonia or any acute infectious reaction. However, the oil was found to be present for several months thereafter.

D Olmer and G Zuccoli (Paris méd 2 306 (Oct 5) 1929) describe a case in which *epileptic seizures* followed shortly after injection of iodized poppy seed oil for the diagnosis of pulmonary tuberculosis. They considered this due to reflex action or to an air embolism through puncture of a small venule on injection of the medium.

A J S Pinchin and H V Morlock (Brit M J 1 930 (May 30) 1931) report several cases of *massive collapse of the lung* following lipiodol injection. Because of its immediate appearance, they believe this is due to a reflex action rather than to blockage of the bronchioles, in cases in which they have produced artificial blockage it has taken from 4 to 6 hours to get the desired collapse.

**INDICATIONS.**—R Schroder and H Jacoby (Arch f Gynak 142 514, 1930) report the use of lipiodol in *pelvic roentgenography*. They find that under normal conditions, injections of from 3 to 5 c c ( $\frac{3}{4}$  to  $1\frac{1}{4}$  drams) of the lipiodol cause no harm to the internal genital tract. These authors feel that hysterosalpingography with lipiodol may be used even in cases that require the genital organs to be left in a normal condition, *e g*, sterility cases. The best time for hysterosalpingography is during the second and third week of the 4-week menstrual cycle. In cases in

which an inflammatory condition is present, lipiodol is nonirritating only in the absence of acute inflammation. In all cases of lipiodol injection, strict asepsis must be carried out.

L Davis, H A Haven and T T Stone (J A M A 94 772 (Mar 15) 1930) report the use of iodized oil in the x-ray diagnosis of diseases of the central nervous system, of the genitourinary tract, the accessory nasal sinuses, cystic cavities, and fistulous tracts, but feel that at present it is being used far beyond the limits warranted. They also report its use as a therapeutic agent but are not impressed with its action. They conclude that localization of spinal cord lesions should be possible by careful clinical study and that injection of iodized oil in the subarachnoid space is dangerous.

**LIVER. — LIVER FUNCTION TESTS.**—*Cinchophen.*—The use of the hepatotoxic product cinchophen has been suggested as a test of liver function by S. S Lichtman (Arch Int. Med 48 98 (July) 1931). The test is based on the theory that the normal liver cell completely oxidizes this substance, while a damaged cell only carries the oxidation process as far as oxycinchophen. A rather simple test for detection of oxycinchophen in the urine has been devised. The dosage used by the author was 0.45 Gm (7 grains). Excretion of more than 100 mgm ( $1\frac{1}{2}$  grains) or 21 per cent of the administered dose of cinchophen was taken to indicate disturbed liver function. In the absence of obstruction, disease of the gall-bladder and ductal system gave normal results. Thirteen cases of *cirrhosis* yielded only 3 normals. *Catarrhal jaundice* gave inconstant results, while in *acute hepatitis* the test was in-

variably positive, the recovery of oxy-cinchophen in the urine corresponding to the severity of the disease. Although the author noted no ill effects following the administration of cinchophen, the toxicity of the drug and the not uncommon occurrence of idiosyncrasy would seem to make experimental investigation extremely desirable before wide-spread clinical use is justified.

**Dextrose Tolerance.**—A modified test of the carbohydrate function of the liver has been suggested by T. L. Althausen, L. Gunther, J. B. Logen and W. J. Kerr (Arch Int Med 46:482 (Sept.) 1930). This test consists of the administration of 20 units of insulin, followed in 20 minutes by 50 Gm ( $1\frac{2}{3}$  ounces) of dextrose and 1500 cc (3 pints) of water. Blood sugars are done at  $\frac{1}{2}$ , 1, 2 and 3 hours. The authors report that in hepatic disease there is a terminal hypoglycemia (below 70 mgm. per 100 cc). Normals rarely reach a figure below 95 mgm. per 100 cc. The height of the hyperglycemia curve is not indicative of abnormality. The test can be applied to *diabetics* with comparable results according to these writers. The explanation offered for these findings is that in normals the dextrose is polymerized to glycogen and released again as dextrose rapidly enough to avoid hypoglycemia. In *hepatic disease* the process is believed to be sufficiently slowed to permit low blood sugar levels.

**Cholesterol Partition.**—In studying 10 cases of *acute parenchymatous diseases of the liver*, E. Z. Epstein (Arch Int Med 47:82 (Jan.) 1931) found that there was a disturbance of the normal ratio between free cholesterol and cholesterol esters in the blood. It is concluded that the normal liver is continually synthesizing cholesterol esters

from cholesterol and fatty acids and reversing the process. In hepatic disease this synthesis does not occur and the ratio between the esters and free cholesterol is reduced. According to this writer 50 to 70 per cent of the normal blood cholesterol of 140 to 200 mgm is in the form of cholesterol esters. In hepatic disease this ratio is definitely decreased, the amount of reduction paralleling the severity of liver damage.

**PORTAL CIRRHOSIS.—Classification.**—A. M. Snell has pointed out that the various forms of cirrhosis which occur from infectious processes such as syphilis, the use of alcohol or of other chemical poisons are much alike clinically and pathologically (Ann Int Med 5 338 (Sept.) 1931). For this reason a clinical classification is difficult to make. Among the clinical types which are reasonably well defined may be included: portal cirrhosis with either hypertrophy or atrophy of the liver, biliary cirrhosis, either primary or secondary to extrahepatic biliary obstruction, pigmentary cirrhosis (hemosiderosis), capsular cirrhosis (polyserositis), and the cirrhosis of Wilson's disease.

**Etiology.**—There are many etiologic agents which are supposed to be capable of causing hepatic injury, but the evidence is largely circumstantial, according to Snell. While about 50 per cent of cirrhotics admit the use of alcohol, only about 5 per cent of marked alcoholics develop hepatic lesions of consequence. However, clinical experience demonstrates some relationship between alcohol and portal cirrhosis, but whether it acts directly or through some intermediary product is unknown. Syphilis may produce cirrhosis indistinguishable from the alcoholic type. At The Mayo Clinic one-fourth of the patients in the



ascitic stage of cirrhosis have had either a positive Wassermann or a more or less definite history of syphilis. In the writer's experience, cholecystitis and infection of the biliary tract are frequently associated with cirrhosis. Other abdominal infections, arsenic poisoning, hyperthyroidism, toxemia of pregnancy, and chronic intoxication from protein and malaria are given as possible etiologic factors.

**Pathology.**—In an effort to determine the degree of vascular reduction in the liver in cases of *cirrhosis* and *Banti's disease*, J. M. Johnston (Ann. Int. Med. 5:773 (Jan) 1931) made measurements of the relative size of the portal radicals. An attempt was made to determine quantitative narrowing of the vessels in cirrhosis and Banti's disease, and to determine the relationship of the degree of narrowing to the size of the spleen, degree of cirrhosis, and age of the patient. Sections of livers routinely removed at autopsy were studied by means of camera lucida drawings. Fields were selected showing satisfactory sections of both portal vein and hepatic artery. The ratio of the arterial lumen circumference to the vein lumen circumference was termed the Ha Pr ratio. The following tabulation shows the results.

Banti's disease are associated with mechanical alterations of the portal blood flow interfering with free exit of blood from the spleen. Younger persons respond to this condition with greater splenomegaly than older persons. In cirrhosis the important factor is not the degree of fibrosis present, but the degree of vascular narrowing. The cause of this vascular contraction is as unknown as is the cause of cirrhosis. The conclusion that Banti's disease is a primary splenomegaly is unfounded, according to this writer.

**Course.**—The course of cirrhosis may be divided into 2 stages: *preascitic* and *ascitic*. Ascites is said to develop in from 50 to 85 per cent. of cases of cirrhosis. The preascitic stage has received little attention, the present study being an attempt to learn something of the earlier symptoms, establish some criteria upon which a prognosis can be based, and study the rationale of medical and surgical treatment. Three hundred and ninety-nine cases were studied of which 135 were cases in which nodular cirrhosis was discovered in the course of abdominal surgery for other lesions, 152 were cases in which the diagnosis of preascitic cirrhosis was made clinically, and 112 were cases of ascites or in the terminal stages. The incidence of cir-

Groups Studied	Average Ratios	Per Cent. Reduction of Vascular Capacity of the Liver
1. Normals ..	1:60	29.0
2. Cirrhosis (spleen less than 300 Gm) . . .	1:43	43.5
3. Cirrhosis (spleen more than 300 Gm) . .	1:34	
4. Banti's disease ..	1:28	53.0

The degree of hepatic fibrosis was found to have no definite relation to the degree of vascular capacity contraction.

Johnston concludes that those conditions known as splenic anemia and

rhosis is indicated by the fact that these 399 cases were obtained from a total of 400,000.

In the first group, 135 cases discovered at operation, the preoperative symp-

toms included typical gall-bladder colic in 30; upper abdominal pain with soreness and "indigestion" in 28, and typical peptic ulcer history in 17, in 10 of whom gastrointestinal bleeding had occurred. Operative findings showed cholelithiasis, duodenal ulcer, and Banti's disease to be the most frequent associated conditions, in the order named.

The second group of 152 cases were diagnosed clinically mainly on a history of alcoholism or syphilis associated with a large liver or spleen and a definite retention of dye. The most common complaints were vague abdominal pain, gaseous indigestion, weakness, and intermittent jaundice, which was usually quite painless. There was a moderate retention of phenoltetrachlorophthalein or bromsulphalein in most cases.

All of the 112 patients in the ascitic group had well marked ascites. The diagnosis was confirmed at operation in half of the cases. The predominating symptoms in order of their frequency were: flatulent indigestion, jaundice, abdominal pain, weight loss and weakness, ascites, diarrhea, hematemesis, anorexia, vomiting, edema, abdominal mass, pruritus. Hernia was present in 47 patients, 50 per cent of the 112 had more or less marked collateral circulation, the liver was palpable in 60 per cent.; and the spleen palpable in about 40 per cent. of cases. About 25 per cent. had some elevation of serum bilirubin, and 40 per cent. had a definite anemia. Dye tests were done in 87 cases with positive results in 80. The retention of dye seems to indicate in a general way the degree of parenchymal injury, according to this author. Prognostically the dye test seems to be of value since those patients with slight retention have a much more favorable course than those with marked retention.

**Prognosis.**—The prognosis of portal cirrhosis is grave in any stage of the disease, Snell states. Of the 112 patients with ascites reported in the paper, 84 have died. Coma, gastrointestinal hemorrhage, and intercurrent diseases were the principal predisposing causes of death. The average duration of life was about 16 months after the appearance of the ascites. The 28 patients still living have survived, on an average, about 38 months after the development of ascites, representing considerable improvement over earlier statistics giving the usual duration of life as 2 to 5 months. The prognosis, according to this writer, can be roughly determined by 4 factors. (1) the degree of retention of dye, (2) the response to treatment with diuretics, (3) the general state of nutrition of the patient, and (4) the presence or absence of complicating disease.

**Treatment.**—Snell (*loc cit*) believes that treatment in portal cirrhosis should be directed primarily toward the detection and eradication of etiologic factors, and secondarily toward the maintenance of the functional integrity of the hepatic cell. Of the 112 patients with ascites 84 were treated with mercurial diuretics combined with ammonium salts in large doses, after the method of L. G. Rowntree, N. M. Keith and C. W. Barrier (Novasural in treatment of ascites in hepatic disease. J. A. M. A. 85: 1187 (Oct. 18) 1925). All were given a high carbohydrate diet, and salt and water were markedly restricted. In 47 per cent, the results were excellent, in 32 per cent they were moderately satisfactory, and in 21 per cent they were poor. According to the author, elderly and cachectic patients should be treated with caution, if at all. The daily use of glucose intravenously

has given excellent results in impending hepatic insufficiency, according to Snell. If patients do not react to diuretics, and are progressively failing, it is unlikely that they will experience any relief from operation, the author states. However, in young patients who are in good condition and respond well to diuretics operation such as **omentopexy** or **splenectomy** should be seriously considered.

### **OBSTRUCTIVE JAUNDICE.—**

**Diagnosis.**—According to W. Walters (Ann Surg 93 1137 (June) 1931), in cases of obstructive jaundice it is of primary importance to determine whether the obstruction is due to a non-surgical lesion within the liver or to a surgically removable lesion in the bile ducts. In most instances this is not difficult. In cases of intrahepatic jaundice there is usually no pain. The general condition may be good, considering the depth of the jaundice, or very poor because of terminal stages of atrophy of hepatic cells. The presence of bile in the intestinal contents can be determined most accurately by nonsurgical drainage with the Lyon tube. In 86 per cent of cases of obstructive jaundice due to stones there is a definite history of biliary pain or colic. The jaundice is variable; it usually appears immediately following the colic, and frequently is accompanied by chills and fever. In the presence of carcinoma of the head of the pancreas obstructing the common bile duct and of stricture of the common bile duct, the occurrence of pain is determined by the degree of the obstruction and the amount of infection in the biliary passages.

**Preoperative Treatment.**—Observation for a few days in the hospital prior to operation is of definite advantage in obstructive jaundice. It gives an opportunity for a regimen of

preoperative preparation to be carried out and for the progress of the jaundice and the condition of the patient with painless jaundice to be evaluated, thereby facilitating the decision as to the necessity for operation.

The intravenous administration of a **solution of calcium chloride** is of definite value in these cases for the *prevention of postoperative hemorrhage*. The *van den Bergh test* is indicated to determine the progress of the jaundice as it is unwise to operate on patients whose jaundice is increasing unless operation cannot be delayed. A coagulation time of more than 10 minutes is not a contraindication to operation, but usually indicates that considerable injury has been done to the hepatic cells. Marked injury to the hepatic cells is evidenced also by the presence of subcutaneous hemorrhages or petechiæ. In such cases, in addition to the solution of calcium chloride, a **blood transfusion** should be given prior to operation and repeated as often after operation as is necessary to control the bleeding.

**Surgical Treatment.**—Although general anesthesia allows good exposure of the biliary passages, **spinal anesthesia** has been adopted for most patients with obstructive jaundice because, in addition to giving perfect relaxation and permitting excellent exposure of the biliary passages, it is associated with less operative reaction and does not have the irritating effect of a general anesthetic on the parenchymatous cells of the liver and kidney.

In most cases in which stones are present in the common bile duct the stones may be felt by grasping the duct between the thumb and forefinger. The best probe is the finger, and if the size of the duct permits, the finger should be used to make sure that no stones are

overlooked. After the removal of the stones from the common duct, a T-tube or catheter should be employed, depending upon the desired duration of drainage of the duct. If there is infection in the liver or in the head of the pancreas, it is best to use a T-tube and to leave it in place for 3 weeks or longer. Otherwise a catheter, described by Mayo-Robson as a hepaticus drain, serves admirably to relieve intraductal pressure and is easily removed on the twelfth day following the operation.

If a stricture of the common bile duct is present and there is sufficient normal duct above the stricture to allow anastomosis between this normal portion of the duct and the duodenum, a good result may be expected.

In some cases in which the stricture is localized and small, the section of the duct containing it can be removed readily and the continuity of the duct restored by end-to-end anastomosis.

Obstructive jaundice due to a tumor at the head of the pancreas can be relieved by anastomosing the distended gall-bladder to the duodenum or stomach, depending upon which can be done more easily and with less tension. If the anastomosis is made to the stomach, the presence of bile in the stomach does not produce unusual symptoms. There is no doubt that some tumors at the head of the pancreas are the result of infection, and that relief of the obstruction by **cholecystenterostomy** gives permanent relief.

Walters (*loc. cit.*) believes that when the jaundice is extreme, **cholecystenterostomy** can be done more safely in 2 stages than in 1 stage. He first drains the gall-bladder and from 12 to 14 days later makes an anastomosis between the gall-bladder and the stomach or duodenum.

The *complications* which occur following operations on patients with obstructive jaundice are *hemorrhage* and *renal* and *hepatic insufficiency*. Of great importance in lessening the incidence of postoperative hemorrhage is the selection of the proper time for operating and the preoperative use of some measure favoring coagulation of the blood. A successful outcome is absolutely dependent upon relief of the obstruction.

**Postoperative Treatment.**—Walters believes it is worth while to administer a 10 per cent solution of glucose intravenously to jaundiced patients subsequent to operation as often as such treatment is indicated. At the time that the needle is inserted into the vein for the injection, a small amount of blood may be removed for determination of the coagulation time, a change in the degree of the jaundice, and the concentration of urea in the blood.

**Postoperative Complications.**—F. Bernhard (Beitr. z. klin. Chir., 150:82, 1930), in paying special consideration to *postoperative liver disease*, states that little attention has been paid to death from liver intoxication, which in the cases reviewed was as frequent as death from cholemic hemorrhage. To explain it, Bernhard experimented on animals. He found that glycogen deficiency in the liver is responsible for the development of postoperative liver intoxications and degenerations, and that following mechanical obstruction of the common duct there is disappearance of glycogen, although no noteworthy change in the blood-sugar level may be demonstrable. The decrease in the glycogen content of the liver cells in obstructive icterus is partially explained by the effect of the bile on an increased diastase destruction of liver glycogen. Also, the lack of bile in the bowel and the consequent faulty

absorption of fat results in the burning of increased quantities of carbohydrate and increased utilization of liver glycogen. Glycogen fixation by the liver is disturbed by the bile obstruction, but is not entirely arrested. Insulin and glucose infusions will increase glycogen synthesis, even in bile obstruction, an effect of importance in the prevention and treatment of glycogen loss in the liver. Early recognition of this condition is possible by the demonstration of urobilin and urobilinogen in the urine. In addition, according to Bernhard's experience, there is a fall in the blood-sugar and a rise in the residual nitrogen before and immediately after the beginning of liver intoxication. As a decrease in the blood-sugar endangers the nutrition of the heart muscle and renders the heart especially sensitive to anesthetics, the administration of glucose and insulin is strongly recommended also for this reason.

**PROTECTIVE RÔLE OF LIVER IN ABDOMINAL SURGERY.**—C G Heyd (Am J Obst and Gynec 19 203 (Feb) 1930) states that in any laparotomy, with or without exposure of the liver, there are a great many possible physical, chemical, infectious, mechanical, and toxemic traumata, plus possible leakage from drainage, plus varying degrees of dehydration. The sum total may often prove fatal to the patient with depressed or impaired liver competency. A significant group of deaths is not due to anatomical causes, infection, overwhelming intoxication of high intestinal obstruction, or perforation. The clinical manifestations of these cases suggest that the death is in large measure due to liver failure or to insufficiency of the protective function usually exercised by the liver.

The liver is notoriously able to control infections and catabolic proteins, the result of infections. If the dosage of these bodies is overwhelming, or their toxicity beyond the detoxifying power of the liver, the latter fails to give protection.

In the presence of persistent vomiting after laparotomy, recourse should be had to blood chemistry determinations. Increase in urea nitrogen, decrease in chloride, and increased carbon dioxide combining power indicate alkalosis as the probable diagnosis. Remedial measures should be adopted before the urine begins to show marked evidence of renal damage. *Treatment* consists of administration of normal saline and glucose through all channels and the giving of acid phosphate solution by mouth or per rectum, the securing of gastric rest by a Levine siphon tube, and jejunostomy if there is evidence of intestinal obstruction or marked jejunal reflex. It is essential to have repeated blood chemistry determinations to control or indicate further therapy. If symptoms of *tetany* appear, 5 cc ( $1\frac{1}{4}$  drams) of 10 per cent. solution of calcium chloride are given intravenously and repeated when necessary.

**LUNGS. — PHYSIOLOGY.**—H Read (Beitr z Klin d Tuberk 76:121 (Nov. 22) 1930) studied thoracographically the *influence of forced mouth-breathing on the movement of the thoracic wall* and demonstrated that a short "transitional reaction" was followed by a reappearance of the rest respiration. Determinations of the carbon dioxide content of the expired alveolar air during and after the mouth breathing revealed that a "respiratory insufficiency" was not produced by

breathing through the mouth. Respiratory experiments with the Knipping apparatus revealed that in most persons there does not occur an appreciable change in the expired alveolar air and in the pulmonary ventilation. In 25 per cent of the cases the carbon dioxide content was increased. Emphasis is laid on the importance of a regular control of the expired alveolar air before and after each experiment.

In an investigation to determine the *volume of blood flow through the lungs following collapse of one lung*, R. L. Moore (Arch Surg. 22 225 (Feb) 1931) recorded the respiratory movements and oxygen absorption curves of the right and left lungs separately in 14 experiments on anesthetized dogs during the inhalation of oxygen. After total occlusion of one primary bronchus and complete collapse of the corresponding lung, similar tracings were taken of the opposite nonobstructed lung. Simultaneous estimations of the oxygen contents of the mixed venous, arterial and aerated blood specimens were made. The data obtained have been used to calculate cardiac output and fractions of blood passing through the pulmonary system of each lung separately, first under relatively normal conditions and, secondly, at varying intervals after bronchial occlusion and complete collapse of either lung. It was found that when breathing was free, the amounts of oxygen absorbed by the right and left lungs, respectively, were approximately in the ratio of 3·2, under similar conditions, the fractions of blood that passed through the right and left lungs were in the same ratio; total occlusion of one primary bronchus was regularly followed by complete collapse of the corresponding lung.

Complete collapse of one lung (either

right or left) was accompanied by a conspicuous decrease in the pulmonary blood circulation on the affected side, the cardiac output and the circulation through the opposite lung decreased to a less extent in 11 of 12 instances, the percentage decrease of blood flow through the collapsed lung varied directly with the decrease in cardiac output. On the basis of these observations the conclusion is drawn that the reduced pulmonary blood flow in a lung that has been completely collapsed by bronchial occlusion results in part from local changes within the lung itself and in part from the accompanying decrease in cardiac output. Of the local conditions, absence of lung motion is probably of some importance.

**PATHOLOGY.**—J. A. Bigler (Am J Dis Child 38 978 (Nov) 1929) studied the lungs of 171 children coming to autopsy to determine what pathological changes were present to account for the shadows seen in the *x-ray of the chest*. The hilar shadows and linear markings were found to be due for the most part to the blood in the blood vessels and not to the bronchi. The rounded shadows of even density occurring in the inner third of the lung fields, as well as those found along the linear markings, were found to have been cast by blood-vessels running parallel with the axial ray. Such shadows changed position or disappeared when the target was centered over a slightly different point of the chest. They were in marked contrast to the shadows of calcified lymph nodes which were always present in the same relative location on successive exposures.

On dissection of the lungs with the films before the examiner, it was found that normal lymph nodes do not cast shadows. Hyperplastic nodes, whether



caseated or inflammatory and whether in the hilum or in the intrapulmonary tissue, cannot be recognized as such if they do not contain calcium. They will not be seen unless they and the inflammation with exudation or scarring which surrounds them encroach on the pulmonary fields from the mediastinum or the hilum, or unless they are rendered visible by contrast with the air-bearing pulmonary parenchyma.

The size and shape of the hilar shadow are influenced not only by active infection, but also by the remains of previous infections. This shadow may show wide variations in different x-rays and yet be within normal limits for the person examined.

**DIAGNOSIS.—Coin or Bell Sound (*Brut d'airain*)**—In reviewing this diagnostic measure, A. I. G. McLaughlin and A. J. Dix-Perkin (*Lancet* 2:1351 (Dec 28) 1929) summarize as follows:

1 The *bruit d'airain* is one of a group of metallic phenomena which may be heard in the thorax under varying conditions. The other members of the group are: (a) Amphoric breath sounds; (b) metallic vocal resonance, either of the whispered or spoken voice; (c) metallic or tinkling crepitations, and (d) the (Hippocratic) succussion splash. All these signs are associated with the presence of an air cavity or cavities in the chest. For the production of tinkling crepitations and the succussion splash, fluid or secretion is a necessary additional factor.

2 The *bruit d'airain* is a clear ringing musical note exactly like that made by striking a sharp blow on a brass vessel (French: *airain* = brass), and it is elicited by listening over the anterior or posterior wall of the chest while an assistant percusses or taps 2 coins to-

gether on the same or opposite wall. Although it is more convenient to use 2 coins, it must be emphasized that the note produced by 2 pieces of wood, or by simple digital percussion, is of exactly the same musical pitch and quality as that produced by percussion with coins, whether gold, silver or copper.

3 Over some pneumothorax cavities a dull, wooden, nonmusical note is sometimes heard. To this sound the term *bruit de bois* has been given by French clinicians.

4 In some cases of **hydropneumothorax** the *bruit d'airain* may be obtained over the air space down to the level of the fluid, but over the fluid itself a higher pitched, fainter, silvery note may occasionally be heard. To this is given the name of the *signe de Pitres* or the *signe de sou*, described by Sieur in 1883.

In diagnosis, the first important point to be observed is that failure to elicit the *bruit d'airain* does not mean that a pneumothorax is not present. Secondly, when the sign is found over the thorax it gives an indication of the presence of an air-containing cavity with tense and rigid walls.

When the mediastinum is displaced the *bruit d'airain* gives an indication of the amount of displacement. For instance, in excessive displacement the sign can be found extending across the spinal column to the side of the uncollapsed lung. In **ballooning of the pleura**, the shape and extent of the bulge can be accurately marked out by means of the *bruit d'airain*. When a **hydro- or pyopneumothorax** is present the sign is heard down to the level of the fluid, and in this way the amount and level of the fluid can be fairly accurately estimated. In this connection the *bruit d'airain* is of much more value

than the percussion note, especially in those cases (usually pyopneumothoraces) where a tympanitic or skodaic note is found over the effusion itself

**ABSCCESS.—Etiology.**—C J Bucher (Am J M Sc 179 406 (Mar) 1930) investigated bacteriologically the pus obtained from 118 cases of lung abscess in the Chevalier Jackson Bronchoscopic Clinic of Philadelphia. In every case the specimen was taken directly from the abscess either by bronchoscopic technic or when the infected area was exposed at operation. The abscesses followed extraction of teeth in 9 cases, tonsillectomy in 40; surgical operations in 9, acute respiratory infections in 16, pneumonia in 17, pleurisy in 1; and were of questionable origin in 23.

The specimens were subjected to staining by Gram's and by Fontana's methods, to dark field examination, to aerobic and anaerobic culture, and in many instances to animal inoculation.

In the individual case usually more than one organism was isolated and occasionally 7 or 8 were recovered. The organism most commonly isolated was the streptococcus, the hemolyticus 34 times, the viridans 44 times, and the nonhemolyticus 15 times. Next in frequency was the *Micrococcus catarrhalis*, then the pneumococcus. The *Bacillus influenzae* and the *Staphylococcus albus* were isolated 41 times and 39 times respectively. Spirochetes and fusiform bacilli were demonstrable in only 25 cases.

The author concludes that it is not possible ordinarily to pick out any one organism as causing the abscess; that the organisms commonly found in the abscess cavity are those found normally in the mouth and upper respiratory tract.

**Prophylaxis.**—In the prevention of pulmonary abscess J Heuer (Surg Gynec Obst 52 394 (Feb 15—No 2A) 1931) advises in all operations, whether about the nose, nasal sinuses, mouth and throat, or elsewhere, that careful and systematic nasal and oral hygiene should be carried out, if possible for some time before operation.

In all operations about the nose, mouth and throat, whether done under general or local anesthesia, great care should be exercised in hemostasis and in measures to remove blood and mucus from the pharynx. The ease and frequency of bronchial contamination and the possible importance of obstructive agents as blood clots and mucous plugs as causative factors in the production of abscess have been referred to.

In all operations careful aseptic technic, the careful handling of tissues, the avoidance so far as possible of the ligation of large masses of tissue are essential to all proper surgery, but they may have an added importance in view of the relationship between septic emboli and pulmonary abscess.

The frequent turning of the patient, pulmonary gymnastics, the encouragement of cough, and the over-ventilation of the lungs with carbon dioxide following operation suggest themselves as preventive measures if the aspiration theory of abscess is favored, and the possible importance of stasis or bronchial obstruction in the causation of abscess is taken into consideration. If the embolic theory happens to be favored, these measures in certain cases may be contraindicated, for as abscess is particularly liable to follow upper abdominal operations and is presumed to be due to the dislodgement of infected emboli, the reverse of these measures—the fixation of the lower chest and

upper abdomen—may seem more desirable and has actually been advocated.

Heuer advises prompt removal of foreign bodies from the bronchi, and, in cases in which operation is indicated, the removal of foreign bodies if possible in wounds of the lung. Both clinically and experimentally, it is the foreign body which produces bronchial obstruction over a considerable period of time which is associated with pulmonary abscess.

He advises the prompt recognition, if possible, and the proper treatment of such acute conditions as mastoiditis and osteomyelitis which give rise to septicemia, and, secondarily, to embolic pulmonary abscess, and conditions such as peritonitis, hepatic and subphrenic abscess which may give rise to the occasional pulmonary abscess by lymphatic extension.

**CARCINOMA.—Incidence.**—P. D. Rosahn (Am J M Sc 179:803 (June) 1930) concludes, from a statistical review of the literature, that primary pulmonary carcinoma is not so rare as was formerly believed, and that its incidence is steadily increasing. Of 3004 adult necropsies performed at the Boston City hospital from 1910 to 1928, 314, or 10.4 per cent, were cancer cases. Primary pulmonary carcinoma occurred in 23, or 0.7 per cent. of all adult necropsies, and 6.69 per cent of all cancers. Combined statistics show that primary carcinoma of the lung discovered at post-mortem examinations from 1910 to 1919 comprised 0.44 per cent of necropsies and 4.39 per cent of all cancers. Since 1920, the figures have been 0.89 and 6.98 per cent respectively. Opinions differ with regard to the question whether this increase, noted by practically all observers, is an absolute one, peculiar to the lung, or only relative to

and coincidental with a general increase in systemic cancer. For reasons which are cited, Rosahn inclines to the former view and considers that because of its increased frequency clinicians should give this affection serious consideration in differential diagnosis in patients of the carcinomatous age presenting puzzling lung symptoms and signs. An early diagnosis will permit of accurate prognosis, and in selected cases, perhaps surgical therapy.

**Pathology.**—W. Boyd (Canad. M. A J 23:210 (Aug) 1930) asserts that there is little to support the theory that inhalation of irritating substances such as exhaust gases from automobiles and tar from roads is a causative factor, and that the apparent increase in the condition can be attributed to the fact that many cases formerly diagnosed as sarcoma or lymphosarcoma are now known to be carcinoma. In 23 cases of primary carcinoma, 14 of which were found in 900 autopsies, tuberculosis and influenza played no part in causing the condition.

Carcinoma of the lung has great invasive power. It usually spreads by the blood stream, frequently causing distant metastases. Of the cases reviewed, secondary growths were found in the liver in 8, the adrenal glands in 6, the kidneys in 5, the brain in 4, the bones in 2, the opposite lung in 2, and the spleen in 1.

According to the gross appearance, 4 types of carcinoma of the lung are distinguished: (1) a tumor arising from the main bronchus and forming a mass at the hilum; (2) a nodule in the lung substance arising from a smaller bronchus; (3) miliary nodules scattered throughout the lung which are due to lymphatic dissemination, and (4) diffuse infiltration resembling pneumonia.

A more satisfactory classification is based on the microscopic appearance. This also shows 4 types (1) the anaplastic or undifferentiated, (2) the medullary, (3) the adenocarcinomatous, and (4) the squamous.

The author points out that silver stains are of value in demonstrating the essentially carcinomatous character of the tumor because epithelial cells are silver-positive, whereas connective tissue cells are silver-negative.

**Symptomatology.**—A. T. Edwards (Brit. Med. J. 1:129 (Jan. 24) 1931) states that the onset of malignant disease of the lung is generally gradual and insidious, but sometimes is initiated by a pyrexial attack commonly labeled influenza. For months, the history in others may disclose nothing except increasing lassitude without localizing symptoms. The symptom is later accompanied by dyspnea or nonproductive cough, both tending to become worse. The diagnosis is the more difficult because the general appearance is often good, and weight may even be gained at this period. Hemoptysis occasionally occurs early. Irregular pyrexia may be an early symptom, but the temperature is rarely high until the later stages, when there is retention of secretions, or when necrosis has occurred in the center of the growth. A sudden attack of hemoptysis, associated with the expectoration of a quantity of purulent sputum, occurs occasionally in malignant disease and tends to confuse the condition with pulmonary abscess, especially as it is often preceded by a rise and succeeded by a fall of temperature. Pain is rare in the early stages but, until the pleura or mediastinum is involved, is never severe. Dysphagia occasionally results from the pressure of secondary deposits in mediastinal lymph nodes on the esophagus and hoarseness

from pressure on, or involvement of, the left recurrent laryngeal nerve.

The signs vary according to the type of the disease. In the *bronchial growth* the physical signs are those of pulmonary atelectasis, bronchial breathing of a blowing type, some dulness and often increase of voice sounds when the obstruction is incomplete, with dulness and weakness or absence of breath and voice sounds when complete bronchial obstruction is present. In the *central or alveolar type*, physical signs may be absent or may consist of localized dulness associated with weakness of breath and voice sounds. Extra-pulmonary signs should also be sought, such as enlarged supraclavicular lymph nodes and paralysis of the homolateral diaphragm due to involvement of the phrenic nerve.

Evidence of venous obstruction, such as dilatation of the superficial veins of the chest and the veins of the upper limb and neck, is comparatively rare in pulmonary neoplasms. Effusions of the pleura are usually late and are often hemorrhagic. Bronchiectasis secondary to the obstruction results in a proportion of cases and its symptoms may mask those of the initial lesion. The fact that the signs are atypical of any of the common lung diseases should immediately suggest the possibility of malignant disease of the lung. Diagnosis may be confirmed by further investigations. These comprise x-ray examination, before and after pneumothorax, and the introduction of iodized poppy-seed oil into the bronchi, bronchoscopy, thoracoscopy and, finally, exploration of the thoracic cavity. In the past, when a diagnosis of malignant disease has been established, the tendency has been to abandon all hope. As diagnosis is becoming possible at an earlier stage, some definite efforts should be made to deal with the

problem of malignant disease of the lung in a more active way than by palliation of symptoms alone

**Complications.**—B M Fried and R C Buckley (Arch Path 9 483 (Feb) 1930) found *metastases* to the central nervous system in 15 of 37 patients with bronchiogenic cancer. For 11 of the 15 patients, a diagnosis of primary tumor of the brain was made, and the bronchiogenic tumor was overlooked. For the remaining 4 patients, a definite diagnosis could not be made. An intracranial operation was performed on 11 of the patients, and a metastatic tumor was removed in 10 instances. The postoperative survival period of the patients with solitary cerebral metastasis varied from 5 months to 7 years. An early postoperative fatality resulted in every patient with multiple cerebral metastasis.

It is believed that when a person of middle age has an abrupt onset of symptoms and signs of a rapidly developing intracranial lesion, a metastatic cerebral lesion should be thought of, and that the lungs are the most common site of the primary lesion. It is realized, moreover, that even in instances in which the examination of the lungs yields negative results, the presence of a primary tumor in these organs cannot be excluded.

A metastasis to the brain from a primary pulmonary tumor was commonly mistaken for a rapidly growing glioma, a cerebral vascular lesion or an encephalitis. Apparently, the pulmonary tumor metastasizes to the brain by way of the blood stream. The relatively great frequency of intracranial metastasis is due in all probability to the fact that a tumor embolus from a pulmonary cancer passes from the pulmonary vein directly into the cerebral circulation, whereas cancers from other viscera on their way to

the brain are primarily retained by the lungs, where they may remain indefinitely, often being altogether destroyed. There is an outstanding reaction on the part of the microglia and astrocytes to the metastatic lesion, the response being very much like that found in experimental studies on the reaction of the brain to wounds and to infectious invaders.

F R Ferguson and W E Rees (Lancet 1 738 (Apr 5) 1930) state that primary carcinoma of the lung is becoming more frequent and probably constitutes 4 per cent of all carcinoma. The increase has been attributed by some to the influenza epidemics and by others to the inhalation of foreign material from the atmosphere, such as motor exhaust gases and the tar used in spraying roads.

Of 29 cases of metastatic tumors affecting the central nervous system which were seen by the authors in the past 3 years, the neoplasms were of pulmonary origin in 9 instances. In the latter, the neurological signs and symptoms were prominent, while the chest signs were few. In the majority of cerebral cases the symptoms are due to an intracerebral deposit, while in the spinal group they are due to pressure on the cord.

These writers assert that there is no syndrome which is pathognomonic of cerebral metastasis. They cite as typical, however, the case of an elderly patient with wasting, which is out of proportion to the extent and duration of the cerebral symptoms, pyrexia, a short history with possibly the sudden onset of a psychosis followed by temporary recovery, radicular pain, vague chest signs or a history of respiratory abnormality, and rapid progression of the condition to a fatal termination.

In conclusion, Ferguson and Rees state that in the examination of patients with an obscure cerebral lesion, it is important to bear in mind the possibility of a metastatic cerebral tumor and make a careful and complete clinical and x-ray investigation

**Diagnosis.**—M. Bagliani (Radiol med 18 214 (Feb) 1931) made an x-ray study of 18 cases of carcinomatous metastases in the lungs. He observed that nodular metastases were more frequent than metastases of the infiltrative type. The nodular forms later became infiltrative, but the primarily infiltrative forms remained unchanged and were never associated with discrete localized nodules. Infiltrative lesions progressed more rapidly than nodular and were often associated with pleurisy.

Both types of metastases were most common in the bases of the lung fields; areas above the hilus were rarely involved.

Under x-ray therapy, with massive doses, the metastases decreased in size more slowly than similarly treated sarcomatous metastases.

**LYMPHOGRANULOMATOSIS.**—H. Weber (Beitr. z. path. anat u z allg. Path. 84 1 (Feb 14) 1930) discusses 7 cases of Hodgkin's disease which had involved the lung. Three of these cases appeared to have their beginning in the lung structure, while 4 others were located within the thoracic glands and had secondarily invaded the lung. Only 1 of these cases was correctly diagnosed clinically, while another was diagnosed by microscopic sections during life. In the remaining group a diagnosis of tuberculosis was usually offered, and in 1 case was found at autopsy to be present along with the nodules of Hodgkin's disease. The granulomatous masses may be small and

local, or may involve the whole lobe. Occasionally multiple, small nodules are scattered through several lobes. The process of necrosis may be more pronounced in Hodgkin's disease of the lung than is usually noted in the lymphatic glands. Cavities may be formed. The structure of the granulomatous mass simulates that encountered in other tissues. The author found that radiation inhibits somewhat the progress of the lesion. The granulomatous mass may give rise to small nodular processes in the intima of vessels. These nodules may develop to obstruct the lumen.

**MILIARY DISEASE.**—R. R. Sayers and F. V. Meriwether (Pub. Health Rep 45 2994 (Dec 5) 1930) report the work done in a clinic established at Picher, Oklahoma, for the study and control of silicosis and tuberculosis among the miners. Physical examination, including x-ray examination of the chest, is made of the men prior to employment and at least once yearly thereafter. A total of 18,285 individuals had been examined up to and including December, 1929. About 125 cases of typical miliary lung disease were found by x-ray examination among these individuals during routine examination. A majority of the affected persons did not have sufficient symptoms to cause them to stop work or seek medical aid. The most characteristic finding was a large number of discrete, dense, shotlike spots scattered over the lung areas. Tubercle bacilli were present in only 2 of the 88 cases in which an examination of sputum was made. Unstained smear of 31 cases (all those examined) were positive for fungi. Two types of fungi were identified, *i e*, *Aspergillus fumigatus-fisheri* and *Aspergillus niger*. Ten cases tested with antigen of *Aspergillus fumigatus-*



*fisheri* gave negative reactions. 6 cases tested with *Aspergillus niger* gave positive reaction. The authors are of the opinion that 38 cases reported by Sutherland as presenting "miliary calcification of the lungs" are probably instances of the same condition as that found at Picher. In addition, they suggest that these miliary calcifications may be due primarily to fungous infection.

**EDEMA.** — *Etiology.* — According to P. Wolfer (Schweiz med Wchnschr 60 885 (Sept 20) 1930), pulmonary edema may be due to various causes. First, he discusses the *mechanical theory*. Experimental investigation of this theory has proved that the purely mechanically caused edema occurs only in rare cases. During heart disease, pulmonary edema occurs but seldom. However, there are other forms of pulmonary edema that are of mechanical origin, *viz*, ventilation edema and edema caused by changes in the thorax.

Wolfer further discusses *inflammatory* and *toxic edema*. The toxic edema may be due either to poisonous products of metabolism or to poisons that are brought into the organism from the outside, such as iodine, alcohol, morphine and particularly gaseous poisons. The condition of the *nervous system* is also an important etiologic factor in some forms of pulmonary edema. In animal experiments, pulmonary edema has been produced by division of the vagus nerve. The fact that pulmonary edema has been observed after trauma of the brain and following inflammation of the spinal cord proves that disturbances in the central nervous system may likewise be significant in the etiology of pulmonary edema. Not all forms of pulmonary

edema can be traced to one of these factors. In many cases, several of the factors are involved.

**SYPHILIS.** — D. C. Hone and J. M. Ross (Lancet 2 806 (Oct 19) 1929) report a case of pulmonary arteritis together with a review of 23 previously published cases. Of the 24 cases, 16 had a definite syphilitic basis. 2 were syphilitic but with nonsyphilitic histology, 1 followed typhus, and the remaining 5 were primary. Age and history of the patient give the sole clue to the possible luetic origin in those affected. To quote from the author's summary: "It is found that syphilis is by far the most important etiologic factor in older patients. Primary noninflammatory sclerosis of unknown etiology is found in younger patients."

In the syphilitic cases the lesions in the intrapulmonary arteries take the form of an obliterative arteritis, usually most severe in the smaller branches and arterioles. This condition leads to a raised blood-pressure in the lesser circuit. Dilatation and hypertrophy of the main pulmonary artery follows with atheroma of the right and left pulmonary arteries and larger branches, whether the latter show inflammatory lesions or not. The right side of the heart becomes greatly dilated and hypertrophied. Clinically, the cases are characterized by dyspnea, cyanosis, and hemoptysis, and in the later stages by progressive congestive heart failure with a regular pulse. *Syphilitic arteritis* of the pulmonary arteries, while admittedly rare, is worthy of notice, since by early diagnosis, **antisyphilitic treatment** might afford some hope of amelioration of the symptoms.

## M

**MALNUTRITION IN CHILDREN.—ETIOLOGY AND PATHOLOGY.**

Malnutrition and hyperactivity are symptoms which frequently occur simultaneously and the relationship of these 2 findings, together with the metabolism of the patient, was the basis of a study by J R Wilson, S Z Levine and M Kelley (Am J Dis Child 39 736 (Apr) 1930). They noted that infants who were 8 to 60 per cent below the average weight were more active and cried more than normal, well-nourished children. The suggestion was made that the extra energy spent by certain malnourished infants might interfere with their utilization of food intake for growth. The measurements of the metabolic rates, however, indicated that this group of infants did not expend energy at any greater rate than a normal group of infants who were equally active and the authors concluded that repeated attacks of gastroenteritis or parenteral infections are more likely to be the cause of malnutrition.

In a study of the metabolism of 12 normal and 14 undernourished children G. Careddu (Riv. di clin pediat 28. 553 (July 28) 1930) observed that the metabolic rate was higher in those children who were gaining height and weight than in those who were losing weight or were stationary, regardless of the state of nutrition. The author considered the metabolic rate to be an index of the probability of a child gaining or not gaining weight within the immediate future.

The problem of anorexia and loss of weight in children has been investigated recently from the standpoint of analyses of the gastric contents, stool examina-

tions and x-rays of the gastrointestinal tract, by M Loeber and H L Weinberger (Am J Dis Child 42 767 (Oct) 1931). Of a series of 36 malnourished children, 20 were found to have hyperacidity of the stomach secretions and 1 of these had a gastric ulcer, 1 a duodenal ulcer. Three children had hypoacidity, 2 children were diagnosed as having spastic constipation, 19 had evidence of faulty starch digestion and 6 faulty fat digestion. Symptomatic treatment in each instance, *ie*, alkalis given to those with *increased acidity*, acids to those with *hypoacidity*, reduction of fat to those showing *fat indigestion*, etc., produced favorable results in most instances.

A reduction of gastric motility in malnourished asthenic children was noted by A Rupp and F W Schlutz (*Ibid* 39 241 (Feb) 1930). By inserting into the stomach of such a patient a rubber balloon and inflating it, they were able to measure the stomach contractions with a manometer. In 11 malnourished children, there were longer periods of low activity of the stomach and the total number of contractions was less than that observed in 5 normal children. Patients with definite gastrointestinal complaints likewise had decreased stomach motility.

The pathologic changes which occurred in 50 patients who died of marasmus have been listed by J Ito (J. Pediat (Tokyo) 349.999 (June 20) 1929). He observed vacuolation of smooth muscle cells in all parts of the body, degeneration and reduction of the number of cells in the Auerbach plexus, structural defects and atrophy of sympathetic nerve ganglion cells, atrophy of the lymphatic system, decrease of

amount of fatty and glycogen containing tissues, and an increase of hemociderin and fat deposits in the liver and spleen

The relationship between *malnutrition and the glands of internal secretion* has been a subject of many investigations. Two studies of the pathology of these glands in patients with malnutrition have been reported recently. In the observation of a group of children in Moscow on starvation diets for 2 to 3 years, W. H. Stefkó (Am J Dis Child 41:1247 (May) 1931) reported an involution of all the glands of internal secretion, with an associated parenchymal degeneration. In a series of animal experiments, J. Rabinowitch and S. H. Gray (Am J Path 6:75 (Jan) 1930) observed that guinea-pigs which had been brought to a considerable degree of malnutrition by starvation had evidence of a failure of proliferation and growth of the thyroid gland substance.

Attention has been called to the fact that malnutrition very often may be due to chronic disease of insidious nature. H. Heiman and P. Cohen (Arch Pediat. 47:537 (Sept) 1930) cite 4 patients diagnosed only as "malnutrition," who were found to be suffering from definite illnesses, 2 with tuberculosis, 1 with syphilis, and the fourth with a lung infiltration, possibly an epituberculosis.

**TREATMENT.—Dietary.**—The most apparent method of treatment of patients with malnutrition has been along the lines of increasing or readjustment of the diet. Many conflicting opinions still exist in regard to the exact character of such treatment. W. P. Lucas and H. B. Pryor (Am J Dis Child 41:249 (Feb) 1931) report the results of dietary treatment of a group of 110 undernourished children many of

whom had complaints of constipation, irritability or fatigue. The food given was low in fat, had a small amount of residue and a high vitamin content. Milk was omitted from the diets and a quart of fruit juices substituted. Additional hours of rest also were prescribed, especially for the hyper-irritable children. Favorable results were reported with this combined treatment, constipation was alleviated, and good gains in weight and height were made. The behavior of the children improved, they were less irritable, and more cheerful in disposition.

A somewhat different diet was used with success by L. C. Rosenberg (*Ibid* 41:303 (Feb) 1931) in the treatment of a selected group of children. He chose 50 children who were undernourished with no severe concomitant disease and fed one-half of the group on a special diet consisting of considerable amounts of vegetables, fruits, cereals and milk, but low in meat and eggs. The other 25 children of the group served as a control and were given an average diet. At the end of 6 months the members of the first division gained 32 per cent more weight and 24 per cent more height than the control series. The specially-fed children attained greater chest diameters, greater leg and hip development and firmer subcutaneous and muscle tissue. The urine of the patients on the special diet was much less acid than that of the control group, there was a greater retention of nitrogen in the special series, the stools were of better consistency and contained fewer and a less varied intestinal flora. The author attributed part of the success of this diet to its high vitamin B content.

Whole wheat germ with its high vitamin B value was advocated as a

growth producing food by A F Morgan and M M Bairy (*Ibid* 39 935 (May) 1930) They fed to a group of children, 11 to 13 years of age, a 3-ounce roll made of whole wheat germ (50 per cent) and white flour (50 per cent) During the periods when this food was taken the children gained 3 times as much weight as during control periods

A diet of vegetable foods selected with a view to providing a variety of proteins and many vitamins and relatively high in carbohydrates, but with the elimination of many fatty foods, milk and meats, produced satisfactory gains in weight during 10 weeks' administration to a group of malnourished children 7 to 15 years of age, according to E Lane and F H Bosshardt (*Ibid* 40 285 (Aug) 1930)

J C Eby (South M J. 23 842 (Sept) 1930) merely fed 2 glasses of milk and 2 bananas as an addition to the lunch of undernourished children and yet observed favorable increases in weight.

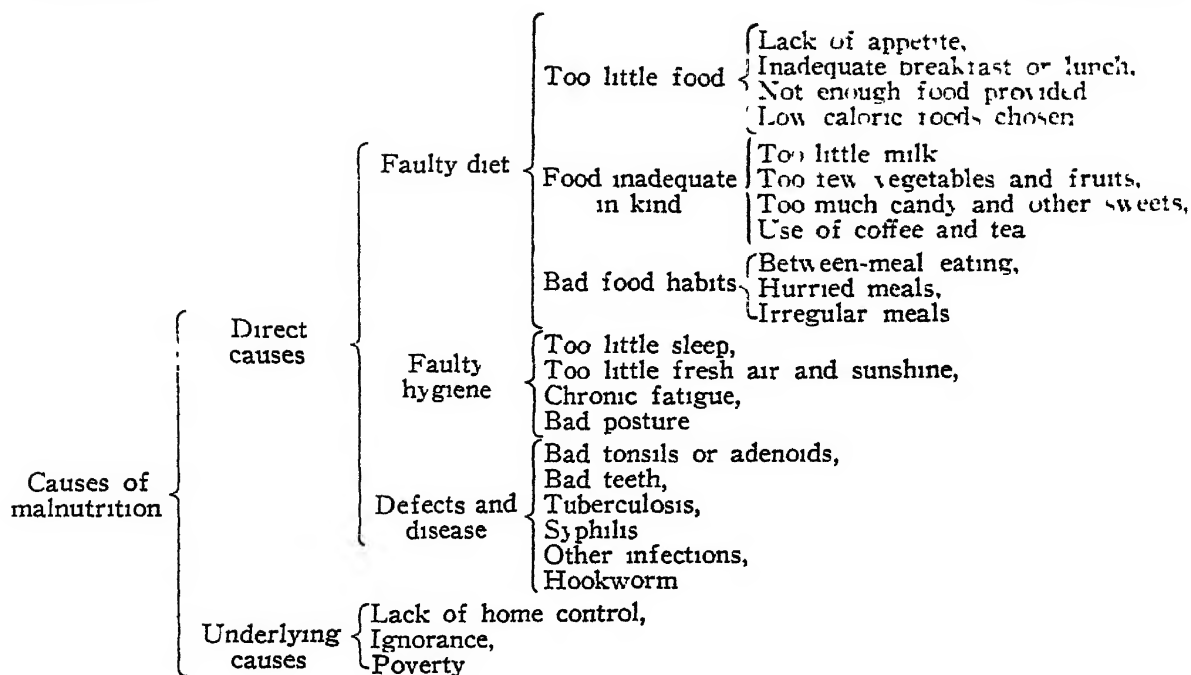
In regard to the feeding of malnourished *infants*, good results were reported by J. H. West (Arch Pediat 48:189 (Mar) 1931) He prepared a mixture of evaporated milk (4 ounces—120 cc), calcium caseinate (3 tablespoonfuls), baked wheat flour (2 tablespoonfuls), and water (28 ounces—840 cc), and the final preparation contained proportions of 38 per cent protein, 125 per cent lactose, 10 per cent fat and 30 per cent starch A group of 152 marasmic infants who were given this diet made satisfactory progress in growth and development As a patient improved, more sugar, milk or fat was added to his formula

Citric acid milk has been advocated as a food for *infants* who are underweight by H Weissenberg (Arch. f.

Kinderh 90 288 (June 27) 1930) In his experience it has certain advantages in that (1) it is easier to prepare than buttermilk or Eiweissmilk, (2) the milk is changed very little in its chemical proportions or physical characteristics, (3) it is a suitable and safe milk to prescribe for atrophic ambulant patients, (4) the feeding need not be changed frequently but merely increased in quantity when necessary, (5) it is not necessary to dilute the acidified cow's milk for infants during the first 4 months of their life Fat and whey were not found to be dangerous ingredients of infant food (6) Full caloric value may be given with whole acidified milk, and atrophic children need a more concentrated food In a series of 128 malnourished infants with diarrhea, none were given preliminary periods of starvation nor were they put on tea alone, but they were treated with citric acid milk from the onset

[From a review of the varieties of dietary treatment of malnutrition, all of which have given good results, it might be concluded that the necessary factors seem to be a sufficient quantity of a diet which is well balanced in carbohydrates, protein and fat, and containing a sufficient vitamin content If such food is taken at regular intervals, and abundant rest is provided throughout the 24 hours, an improvement in nutrition may be expected ]

Statistics indicate that about 20 per cent of the children in this country can be graded into groups of malnourished This alarming condition is due either to the lack of adequate food for nutritional requirements, or to the inability of the body, through physiological or environmental interference, to utilize definite food constituents for growth, maintenance and repair The erroneous idea



that only underweight is a criterion of malnutrition must be corrected, as both underweight and overweight individuals are malnourished at times. Although underweight, as a rule, is due to malnutrition, cases may be encountered in which the weight and height are normal but the physical and mental functions are below par, due to some diet deficiency.

In the case of the *obese*, malnutrition is common, due to the diet which may supply an abundance of calories but inadequate tissue building materials, *i.e.*, protein, vitamins and minerals, known as body regulators. This class includes particularly *babies*—fed entirely on proprietary food whose high caloric value is instrumental only in increasing the weight; *children*—whose dietaries of cereals, sweets, bread and coffee are mostly of concentrated refined carbohydrates; and *adults*—who live on an abundance of potatoes, white bread and cereals.

Beriberi, scurvy or rickets are outstanding types of malnutrition. At present, interest is centered on the

causes of certain indefinable states of ill health, such as vague gastrointestinal troubles, loss of appetite, loss of weight, vigor and stamina, poor bone development, instability of the nervous system, and lack of resistance to disease which have a connection with malnourishment.

An excellent outline by Bogert ("Nutrition and Physical Fitness," 1931) indicates some of the interrelated causes of malnutrition.

In endeavoring to correct malnutrition, the physiological and environmental causes should first be remedied, as they have an adverse effect upon the body gaining full advantage of the improved diet. The diet should be adequate in **protein** of good quality (meat, eggs, cheese, milk, fowl); in **minerals**, particularly iron, calcium, phosphorus and iodine, to meet the insufficiency in blood and bones; in **vitamins** to aid in regulating the gastrointestinal troubles (vitamine B), protection against infection (vitamine A), improvement in growth (vitamine A) and dentition, in this case particularly foods rich in (vitamines C and D).

HIGH CALORIC DIET FOR MALNUTRITION  
CHARACTERIZED BY

- 1 High caloric intake, 500 to 1000 grams in excess of body needs
- 2 Adequate amount of good quality protein, approximately 75 grams daily
- 3 Supplied with essentials—minerals iron, phosphorus and calcium, vitamins A, B, C, D, and E

Suggestions for adding foods to increase calories:

- 1 Use butter and cream in liberal amounts
- 2 Give foods requiring the addition of cream and sugar
- 3 Use mayonnaise and its variations with salads
- 4 Use jam and jelly frequently
- 5 Give high caloric beverages between meals
- 6 Lactose in addition to cane sugar may be used for sweetening

Through the day it is found advisable to include in the day's menu

Milk, 3 to 4 glasses

Cream,  $\frac{1}{4}$  pint

Fruit, 3 times a day.

Vegetables, cooked and raw, twice a day

Cereal in the morning

High caloric beverage at 10 30, 3 30 and 8 o'clock

Average serving of meat once or twice a day

Eggs, 1 to 2

*Sample Menu*

Breakfast	Fruit, $\frac{1}{2}$ cup Cereal, $\frac{1}{2}$ cup Toast, $1\frac{1}{2}$ slices Butter, 2 squares Bacon, 3 strips Cream, 1 ounce Sugar, 2 teaspoonfuls Jelly, 1 tablespoonful Milk and cream (1 ounce cream in 1 glass of milk), 1 glass
10 30	Milk and cream
Dinner	Soup, $\frac{1}{2}$ cup Meat or substitute, 1 serving (75 Gm) Potato, $\frac{1}{2}$ cup Gravy, 2 tablespoonfuls Hot vegetable with butter, $\frac{1}{2}$ cup Bread, $1\frac{1}{2}$ slices.

Dinner	Butter, 2 squares
(cont)	Salad with mayonnaise, $\frac{3}{4}$ cup Dessert with cream, $\frac{5}{8}$ cup Milk and cream, 1 glass

3 30 Fruit juice and graham cracker

Supper Same as dinner

The above diet furnishes 3000 to 4000 calories, depending upon size of servings taken

**Glandular Therapy.**—Infants with marasmus have been treated in previous years with internal gland preparations with varying success. Recently P Nobécourt, R Liège and M Guérin (Arch de méd d enf 33 647 (Nov) 1930) observed increases in growth and nutrition of 5 infants treated with **thyroid extract**. The authors believe the water metabolism of the infant is favorably affected by this treatment

**Insulin** has been employed with success in the treatment of adults who were malnourished, according to the report of R D Metz (J A. M A 96 1456 (May 2) 1931). He administered insulin by subcutaneous injections of 20 units  $\frac{1}{2}$  hour before each meal. Many patients gained considerable amounts of weight, slept better and were brighter mentally. The treatment was continued for the period of 1 month. The patients were carefully observed for *symptoms of overdosage*, which were generally a rapid pulse, blurring of vision, tremor of the hands, intense hunger and thirst. Many patients learned to recognize the signs and to treat them by taking **sugar** or **orange juice**. The prolonged use of insulin is more difficult in children, but when it is possible to maintain constant observation, the method might be employed for the treatment of malnutrition.

G Careddu and L. Giua (Riv di clin pediat 28.487 (June) 1930) administered insulin to a group of 14 undernourished infants, mostly under 2 years



of age Three units were given each morning together with 25 to 35 Gm ( $6\frac{1}{4}$  to  $7\frac{1}{2}$  drams) of beet sugar This treatment was well tolerated by the infants and they made gains in weight of 11 to 40 Gm ( $2\frac{3}{4}$  to 10 drams) daily

**MATERNITY CARE.**—L I Dublin and H Corbin (Am J Obst and Gynec 20 877 (Dec) 1930) report a study made jointly by the Maternity Center Association and the Statistical Bureau of the Metropolitan Life Insurance Company of the records of 4726 women supervised by the Association during the past 8 years

Only 28 per cent of the patients came under observation before the fifth month of pregnancy About 50 per cent of the women were delivered at home Physicians attended a little more than 75 per cent of all cases, Bellevue Midwife Service 17 per cent, and other midwives 7 per cent

The following interesting observations are reported

1 During the entire 8-year period no woman under supervision expired before delivery

2 Eleven mothers died after delivery from puerperal causes

3 There were 4596 live babies, 123 stillborn, and 132 babies died before they were one month old

4 There were 274 premature deliveries, 61 of which were miscarriages The maternal mortality was reduced to about a third of the mortality occurring in the same area among women not receiving intensive prenatal care Stillbirths were 42 per cent lower than in the rest of the district, and the infant mortality in the first month was reduced 32 per cent as compared with the control group in the same area, further proof of the value of prenatal care.

These results speak well for the efficacy of the methods of the Maternity Center Association

**MEASLES (RUBEOLA).—ETIOLOGY.**—Although several investigators have produced evidence that a streptococcus is the etiologic agent of measles, the conclusion has not been universally accepted In the tropical countries, measles is quite common, but the ordinary streptococcus infections are rare This is accepted as evidence by P M Otero and E B McKinley (Porto Rico J Pub Health 5 36 (Sept) 1929) that measles is not a streptococcus disease They also injected blood from 6 measles patients into monkeys and the symptoms of measles developed in the animals No microorganisms could be found in the human blood nor in the blood of the monkeys which had been inoculated and had contracted the disease

**SYMPTOMS AND SIGNS.**—An early sign of measles, appearing 2 or 3 days before Koplik's spots, has been noticed by G Petenyi (Monatschr. f Kinderh 45·61 (Sept) 1929). Small *hemorrhagic spots appear on the mucous membranes of the mouth* especially on the soft palate and less numerous on the interior of the cheeks, and are present for several days Of a group of 14 patients observed during the prodromal stage of measles, this punctate exanthem was found in 6 instances

Observation of 29 patients during their incubation period of measles revealed several more or less constant findings, according to P Lereboullet and P. Baize (Arch de méd. d enf. 34:475 (Aug) 1931). Eleven patients had an *elevation of temperature* during the incubation period, usually only a degree or less but sometimes a higher fever of

short duration. Only 3 children *lost weight* during this period and 4 remained stationary. The *leukocytosis* described by previous authors as occurring in this incubation time was in general confirmed in the counts made on 7 patients. There were 12,000 or more white blood cells, mostly polymorphonuclear neutrophils, the maximum increase being reached usually on the sixth to the eleventh day and falling rapidly with the appearance of the symptoms of the invasion period, with a still further decline when the rash developed.

An *enlargement of the spleen* is often considered as a fairly common occurrence in patients with measles, but E. Friedman (Am J Dis Child 42 1114 (Nov) 1931) was able to palpate the organ in only 10.8 per cent of a group of 119 children with the disease. In only 4 patients was it greatly enlarged. The size of the spleen bore no relation to the severity of the attack of measles nor to the occurrence of complications. In a previous series of measles patients examined by the author, only 12 per cent of the children had been found to have palpable spleens.

The *effect which sunlight* has on the development of the rash of measles was reported by P. Woringer (Strahlentherapie 39 493 (Jan 31) 1931). He treated a group of children who were in the incubation period of measles with sunlight radiation. One part of the body of each patient was covered with a black cloth and the other part left exposed to the sun. The rash developed sooner on the exposed portion of the body, was more intense in its color, and it disappeared more quickly than the rash occurring on the protected areas of skin. Sunlight was thought to hasten the production of immune bodies and to in-

crease the activity of the protective functions of the skin.

**COMPLICATIONS.**—Measles may have a deleterious effect on patients with active *tuberculosis* and may also light up old latent tuberculous lesions. This relationship between the 2 diseases has been the subject of study by P. Nobécourt, R. Liège and A. Herr (Arch de méd d enf 33 65 (Feb) 1930). Among 459 children with measles, 33 or 7.18 per cent, had positive skin reactions to tuberculin. Only 15 or 3.48 per cent developed active tuberculosis immediately after the measles attack. However, among the number of children suffering from tuberculous meningitis, 62 per cent had a history of measles a short time before. In a group of 4 children between the ages of 2 and 5 years who had active tuberculous lesions and contracted measles, all died, 3 of pneumonia and 1 of a hemiplegia. It was questionable whether the tuberculosis had been directly responsible for the complications or whether it had acted only in an indirect fashion by lowering of body nutrition and resistance.

An x-ray study of the condition of the *lungs* of patients with measles was made by J. L. Kohn and H. Koiransky (Am J Dis Child 41 500 (Mar) 1931). In x-rays of a group of 130 children with measles, shadows suggesting pulmonary infiltration occurred in 62.4 per cent of the patients below 4 years of age and in 42.2 per cent of the group above 4 years of age. Thirty-two children of the younger, and 24 of the older group were observed again 6 to 10 months later. The most constant finding in both the acute stage and several months later was pleural involvement, represented in the later x-rays by pleu-

ial thickening, which was frequently interlobar. However, empyema had developed in only 1 instance. The increase of the hilar shadows, noted frequently during the measles attack, was not seen 6 to 10 months later. This temporary widening was thought to be due possibly to engorgement of the great vessels and a temporary increase in the size of the lymph nodes. Exaggeration of bronchial marking, noticed so frequently in x-rays of the lungs during the acute attack of the disease, had generally disappeared by 6 to 10 months.

*Pulmonary edema* as a complication of measles was observed in 4 patients by P. Nobécourt and J. Lereboullet (Arch de méd d enf 34 461 (Aug) 1931). The symptoms were typical, consisting of a frothy saliva, dyspnea, cough, cyanosis, a rise in temperature, diffuse râles throughout the chest, and a rapid heart rate. It usually developed at the height of the exanthem or a few days later. In contrast to bronchopneumonia, pulmonary edema often may yield to treatment which consists of the administration of **oxygen**, **cardiac stimulation** and, occasionally, **bleeding**. Considering the time of appearance of this complication and the absence of any other complication, the authors thought that the virus of measles was probably responsible for the lesion.

The *encephalitis* which occurs as a complication of measles may be primarily cerebral in its manifestations, or spinal, or a combination of both. J. G. Greenfield (Brain 52 171 (July) 1929) differentiates the symptoms of each. With the *cerebral form*, patients usually have a secondary rise in fever, somnolence, possibly delirium or convulsions. Signs of meningeal irritation often accompany this type and choked optic

discs may be observed. The acute stage is passed within a few days but changes in behavior and temperature sometimes remain. The *spinal form* of this complication is less frequently attended by a rise in fever. It is characterized by paralyzes, usually flaccid in type, affecting the lower part of the trunk and the legs, with some involvement of the sphincters. Pain and temperature sensations are more often affected than that of touch. Pathologic changes observed in the brain and spinal cord include acute congestion, petechial hemorrhages in some instances, round cell infiltration about the vessels and areas of demyelination. These findings are very similar to those present in the central nervous system of patients with post-vaccinal encephalitis.

A pathologic examination of 6 patients who died with *central nervous system* complications of measles was made by A. Ferraro and I. H. Scheffer (Arch Neurol and Psychiat. 25 748 (Apr) 1931). The outstanding lesion was a perivascular infiltration consisting mostly of "micro-glial" elements, or occasionally of lymphocytes or plasma cells and sometimes petechial hemorrhage. This reaction occurred mostly in the region of white substance but likewise, to a lesser extent, in the cortical regions. Demyelination and axis cylinder involvement were frequently noted. Definite changes in the blood-vessels, consisting of edema or hyperplasia and the presence of thrombi led to the conclusion that the toxic agent was carried to the brain by the vascular system. Mention is made of theories to account for the occurrence of encephalitis in certain diseases, such as measles, smallpox and vaccinia, viz., (1) that the central nervous system complication is

due directly to the virus which causes the primary disease, (2) that it is due to an allergy or anaphylaxis produced by the preceding illness, or (3) that some unknown virus is activated by the acute exanthem and attacks the brain or spinal cord

The effect of measles on the *vegetative nervous system* was studied by L. Kostyál (Ztschr f Kinderh 49 605, 1930). He injected adrenalin at various stages of the disease and observed the intensity of the reactions to this drug, concluding that there is a condition of vagotonia at the onset of the symptoms and with the appearance of the rash. At this time there was noted an increase in the calcium of the blood serum, with a diminution of the potassium. Later in the disease the sympathetics were thought to become hyperactive.

The same question of the effect of measles-toxins on the *suprarenal glands* and on the *circulatory apparatus* has been investigated by G. Macciotta (Clin pediat 13 349 (May) 1931). He has observed measles patients with definite symptoms of adrenal insufficiency, such as disturbances of metabolism of sugar, low blood-pressure and irregularities of rate and rhythm of the heart. The symptom of laryngospasm which frequently occurs in measles occasionally was attributed to vagotonia. In several necropsies, destruction of the suprarenal tissue was noted.

The incidence of foreign invading microorganisms in the *pneumonia* which occurs as a complication of measles has been the subject of numerous investigations. In recent epidemics in London, J. B. Ellison (Arch Dis Childhood 6: 37 (Feb)) 1931) observed the influenza bacillus in 46 per cent of 24 pa-

tients with measles pneumonia. The streptococcus, pneumococcus and staphylococcus were also found, either alone or associated with each other. Hemolytic streptococci were quite rare, especially in children. The pathologic examination of the lungs gave evidence of an interstitial pneumonia in many instances and this lesion was attributed to the influenza bacillus.

Very characteristic pathologic lesions occur in the *tonsils* and *mucous membranes* of measles patients, according to A. S. Warthin (Arch Path 11 864 (June) 1931). Histologic examination of the tonsils which had been removed from 4 patients 1 to 4 days previous to the appearance of a measles rash revealed an infiltration of multinucleate syncytial giant cells, lymphocytes and monocytes just below the epithelium. The mucous membrane was swollen and congested and the above mentioned cells had migrated into it. Certain areas which were more acutely edematous and congested, contained aggregations of giant cells and these localities suggested potential Koplik spots. Although the pathologic findings suggested that the etiologic agent of measles resided in the pharyngeal mucous membrane, none of the many staining methods employed revealed the presence of any known microorganism within the giant cells or elsewhere in this tissue. Streptococci of an oval shape were present in great numbers in the tonsillar tissue of all 4 of the patients.

**TREATMENT.**—In regard to the treatment of measles with drugs, no one preparation has found favor universally. Recently, *amidopyrine* has been advocated by G. W. Ronaldson and J. I. Collier (Brit M. J 2 994 (Dec 13) 1930). When given to 150 patients

early in the course of the disease, the drug apparently had considerable effect in reducing the fever and was thought to alleviate the other symptoms. Doses of 1 grain (0.06 Gm.) for each year of age were given up to a maximum of 5 grains (0.3 Gm.). Contrary opinions in regard to the value of amidopyrine, however, were held by W. H. W. Attlee (*Ibid.* 2:996 (Dec. 13) 7930). Nine measles patients treated with the drug were noted to have had more severe attacks of the disease than the average of 120 untreated patients.

**Immunization.**—*Human Convalescent Serum*.—The value of human convalescent serum in the prevention of measles is well illustrated in the report of W. Warwick (*Canad. M. J.* 21:694 (Dec.) 1929). In an institution, 69 children between the ages of 3 months and 4 years were exposed to measles. Within 5½ days after the exposure all of the children received injections of blood taken from adults who had recovered from the disease a few weeks previously. Ten c.c. were given to all but 12 older children and they received only 6 to 7 c.c. Within the next 10 or 11 days several children had symptoms of an upper respiratory infection with a slight discharge from the eyes and nose and some slight fever, but all recovered within a day or two. Five had the above symptoms, and in addition a mild atypical rash but no fever. They were diagnosed as modified measles. None contracted the typical symptoms and rash. The group of children were exposed again to measles 2 weeks after the first exposure and yet none developed the disease.

D. N. Nabarro and A. G. Signy (*Brit. M. J.* 1:12 (Jan. 3) 1931) used convalescent serum in doses of 5 c.c. for

children up to 3 years of age and 7 c.c. for older patients. Among 361 hospitalized children who were exposed to the disease, the injections prevented measles in all but 3 per cent., and in 125 exposed patients living at home, all but 5.6 per cent. were protected. In several of the children who contracted the disease in spite of the prophylactic treatment the injections had been given late in the incubation period, i.e., after the fifth day of the exposure.

By the use of convalescent serum, O. Bang (*Acta paediat.* 10:98 (Aug. 18) 1930) protected 88 per cent. of a series of 152 patients from an attack of measles and witnessed attenuated attacks in 9 per cent. The serum was given on or before the fourth day of exposure, in doses of 5 c.c. for infants 1 year of age or under, 10 c.c. for infants 1 to 3 years of age, and 15 c.c. to older children or adults.

The difficulty of storing convalescent serum for considerable lengths of time in order to have it available when needed has been met by a method described by A. Lichtenstein, of Sweden (*J. A. M. A.* 96:2102 (June 20) 1931). Serum stored in liquid form often loses its potency, but when dried, the material retains its immune bodies for a longer time. A method of drying was first instituted by Wiese and modifications have been adopted by Lichtenstein. The serum collected from 3 donors was tested for sterility and a Wassermann reaction performed. Phenol was added in proportions of 0.5 per cent. and the serum divided into 5 c.c. portions in small wide-necked flasks. These flasks were put in an exsiccator and dried in a vacuum. At the end of 3 days, the material was usually dry and the flasks were corked and stored in a refrigerator.

When needed, the dried material was redissolved in sterile water, this taking about 1 to 2 hours. The presence of phenol was necessary to insure the redissolving of the material. Convalescent serum dried in this manner was found to retain its potency for at least 2 or 3 years.

*Immune Adult Blood*—Since there is only a limited supply of fresh convalescent serum, blood of adults who have had the disease several years previously has been used for the purpose of conferring passive immunity to susceptible children exposed to measles. Excellent results were obtained with this method by A. E. Siegel and H. Ermann (Am J M Sc 179 192 (Feb) 1930). In an institution of 100 children all were exposed to a patient with measles. Fifty-five of the group had no history of previous attacks and each was given an intramuscular injection of 5 cc of serum from a pooled supply obtained from parents who had had measles previously. None of the children developed measles and it was concluded that the administration of the adult blood serum had played an important part in the prevention of the disease.

With the administration of adult immune serum, L. Bivings and R. W. Dickson (South M J 23 880 (Oct) 1930) were able to passively immunize 68.9 per cent of 103 children exposed to measles. The remainder had attenuated forms of the disease. For complete immunization there was instituted a dosage of 0.5 cc of serum per pound of body weight to be given during the first 4 days of exposure.

Less favorable results in regard to the effectiveness of immune adult blood in conferring passive immunity against measles have been reported by S. A.

Blauner and H. Goldstein (Am J Dis Child 42 803 (Oct) 1931). At the outbreak of measles in an institution, 117 children with no previous history of an attack of measles, were exposed to the disease. To 5 children, parents' whole blood was given in doses of 30 cc. Another group of 66 received similar amounts of whole citrated blood taken from 2 professional donors who had had measles previously. Forty-six children received no treatment. The majority of the treated group had received the injection within 5 days before or 5 days after exposure as nearly as could be determined. In the final analysis the immunized group were found to have contracted the disease in a greater percentage (88 per cent of immunized and 60 per cent of untreated groups) and it was also stated that the clinical course was not modified in any demonstrable fashion.

The comparative value of human convalescent serum, immune adult serum, and immune goat serum (Tunncliffe) in conferring passive immunity to various groups of children exposed to measles has been discussed by L. H. Barenberg, J. M. Lewis and W. H. Messer (J A M A 95 4 (July 5) 1930). Adult whole blood, administered in doses of 30 cc to 56 children directly exposed to measles apparently protected 13 and modified the attack in 23. The time of giving the prophylactic material is important. When injected within 8 days before or 5 days after the patient's exposure, the adult blood modified the course of the measles in 23 of a group of 26 children. The complications of the disease were less than one-third as numerous in the treated group than in a control group. Serum from patients recently recovered from measles was a



more potent immunizing agent. Injections of 6 c c of such serum in 64 children exposed to the disease protected 73 per cent and modified the attack in 23 per cent. Those who developed the attenuated forms had no complications. Immune goat serum (Tunnickliff) injected into 30 children in doses of 8 c c within 3 days after exposure did not prevent the disease in any instance nor did it modify the attack.

A somewhat similar comparative study of the value of **immune adult serum** and **convalescent serum** was reported by E. Garrido Morales and O. Costa Mandry (*Am J Dis Child* 39: 1214 (June) 1930). Four to 6 c c of convalescent serum given to 120 children exposed directly to measles protected 85 per cent and modified the attack in all but 4 of the remainder. Immune adult serum given in doses of 20 to 40 c c to another group of 132 children exposed to the disease protected 80.3 per cent, and modified the attack in all but 6 of the remainder. Smaller doses of immune adult serum protected only half of the number of children so treated but usually modified the course of the illness. Of a control group of 183 children exposed to the disease, 81.4 per cent contracted measles. In a comparison of the statistics, convalescent serum or large doses of immune adult serum apparently had definite value in preventing the disease or attenuating the attack if given to the patient soon after exposure. In over 500 serum injections, only 2 patients had any reactions such as fever or urticarial rash.

In order to make **immune adult serum** more potent, attempts have been made to enhance the immune body content by injection into adults of small quantities of measles virus. W. Knoep-

felmacher and J. Stross (*Wien klin Wchnschr* 44: 213 (Feb. 13) 1931) have developed such a technique. Blood is withdrawn from a patient on the first day of his rash and 10 c c of it are injected into the adult. At intervals of 1 to 2 weeks, 2 similar injections are given. A week after the last injection, serum is withdrawn from the donor and after sterility is proven, it is divided into doses of 5 c c and each dose sealed in ampoules. In the prophylactic treatment of 115 patients, this serum in 5 c c doses protected 64 to 72 per cent of the group.

**Animal Sera**—**Normal horse serum** alone, apparently has a beneficial action in protecting children from measles, according to the report of P. Mazzioti (*Riv di clin pediat* 28: 1049 (Nov.) 1930). Of a group of 36 hospitalized patients treated with 5 to 7 c c of this serum, 24 did not contract measles, while 8 of those who did fall sick had attenuated forms of the disease. A similar ratio of protection was observed in another group of 21 patients. Fourteen of this group did not contract the disease, while the 7 who did, had long incubation periods of 16 to 25 days.

The **anti-measles serum** prepared by immunizing goats with the diplococcus isolated by Tunnickliff has been employed in producing passive immunity to measles in children exposed to this disease. The method has met with varying success in the hands of different clinicians. When administered to the patient within the first 4 days of his exposure, it is thought to protect against an attack of the disease. Such were the conclusions of M. G. Peterman (*Am J Dis Child* 39: 294 (Feb.) 1930). He gave the anti-measles horse or goat serum to a group of 77 patients

who had no history of a previous attack of measles and who had been exposed to the disease 1 to 5 days previously. Seventeen patients developed measles, while 50 or 74.6 per cent did not. In only 1 instance was there a severe serum reaction and in 4 patients a moderate reaction.

#### Other Methods of Immunization.

—A novel method of administration of immune measles serum to persons exposed to the disease has been employed by C. Anderson and F. Gerard (Compt rend Soc de biol 104 674 (June 20) 1930). With the idea of producing a local tissue immunity, convalescent serum was dropped into the eyes of susceptible persons who had been in contact with measles. One drop was instilled on the conjunctiva of each eye 3 or 4 times a day for a period of 8 to 10 days. It was assumed that the serum reached the nasal membranes also by this route. All of the patients so treated escaped the disease, at least for an observation period of 18 days after exposure. Other susceptible children not treated contracted the disease after the customary incubation period. No statistics of the number of patients was given.

**MEASLES, GERMAN.** See RUBELLA

**MEGACOLON.** See COLON MEGACOLON

**MÉNIÈRE'S SYMPTOM-COMPLEX.**—The past year has seen a number of interesting articles in the literature on the treatment of vertiginous symptoms in connection with the internal ear. The disease originally described by Ménière, in 1861, was a demonstrable hemorrhage in the semicircular canals of an ear that was hitherto perfectly normal. This original case re-

port was that of a girl who suddenly developed severe tinnitus, accompanied by a profound hearing loss, vertigo, nystagmus, staggering gait, tendency to fall to one side, nausea, vomiting, loss of consciousness and later syncope. Of decisive importance has been the gradually attained perception that *morbus Ménière* is not only a matter of local (hemorrhagic exudate into the labyrinth), but also of general disease, whose extra-aural manifestations exhibit the same capricious changes which characterize the acoustic as well as the vestibular phenomena. While these may vary in individual intensity as to frequency and intensity, they are indeed almost constant.

**TREATMENT.**—For some time it had become evident to D. Dederding (Acta-Otolaryng 16 404, 1931) that, as far as the labyrinth was concerned, an accumulation of fluid (*hypertensio auris internus intermittens*) had to be dealt with, as all previous treatments of merit seemed to be dependent upon an increased output of fluid. By degrees, the general character of the disease became apparent to Dederding and his co-workers. A number of other phenomena were perceived as having their rise in similar accumulations of fluid and they reach the conclusion that these patients really have an abnormal water metabolism. Their patients themselves volunteered the information that they heard best when they were able to perspire, in which case headache and general well being improved. Others declared hearing to be best after having taken exercise (dancing, running, tennis, walks, bicycling and field labor), while they were worse during periods of sedentary occupation, after having partaken freely of fluids, or if the weather was very damp. Forced diaphoresis by

pilocarpine sweats as well as the administration of diuretics did not give uniformly good results, in some instances drugs may produce deleterious effects

**Restriction of the intake of fluids**, thereby emptying the deposit of same in the organism, was the basis of the therapy. By measuring the intake and the output of fluid for some days, they were able to discover the level upon which the patient spontaneously adapts himself. The authors were also guided by the **water metabolism** of the patient as presented by Nielsen (*Acta Otolaryngologica* 16 415, 1931). A test is presented with intake of 1000 cc (1 quart) of water on an empty stomach. Under normal conditions this would all be excreted in the course of 4 hours, all except, at the most, 200 cc. A transitory hydremia of 6 to 20 per cent is found by means of V. Allen's hematocrit. In pathological conditions there arise partly a retention of fluid, partly an absence of this hydremic reaction, and partly a combination of both. This is very evident in acute and chronic infections and also in various constitutionally abnormal conditions such as anemias, obesity, rheumatism, etc. Abnormal reactions also exist in the great majority of Ménière patients, in many of whom a distinct aural reaction, consisting in deafness of the sound conduction type, giddiness and nystagmus is observed.

The **thirst cure** is but one side of the treatment, a **stimulating therapy** being advised for capillomotor stasis or failing vasomotor function. The means which give the best results are **massage, gymnastics, exercise, fresh air, Finsen light, and baths**. Naturally, the treatment must be individualized so that the patient is not weakened, but

skin, muscles, lungs, and the entire vascular system are trained by degrees. The author also emphasizes the importance of a careful medical examination for uncovering the fundamental etiology in each case and the **causal treatment** chosen accordingly in a given patient. Local treatment likewise is not to be lost sight of when indicated. By this dehydrating and stimulating treatment of Ménière patients there is observed, simultaneously with the general improvement of the patient, a distinct change in the reactions on the water metabolism, in so far as the condition relating to the output of fluid and the physiological hydremic reaction approach the normal.

**MENINGITIS.—MENINGOCOCCIC SEPTICEMIA.**—Emphasis upon the blood stream infection in meningococcic meningitis is taken up by R. Middleton and William Duane in an article on *fulminating meningococcic septicemia* without meningitis (*Am J M Sc* 177 648 (May) 1929). He states that the disease is transmitted to the central nervous system by 2 routes, *i e.*, the lymphatic and the hematogenous. The former is considered the more frequent, but recently blood cultures have given positive results oftentimes before evidence of localization of the disease in the central nervous system. In some cases the infection never reaches the nervous system, but remains as a septicemia. The author recognizes 2 types of septic meningococcic infection (1) A prolonged febrile state characterized by arthritic symptoms and mild roseolar eruption, and (2) a fulminating form with widespread purpuric blotches and rapid fatality. He reports 1 case of the latter type in which death occurred within 15½ hours after onset.

*Chronic meningococcic septicemia* usually begins rather suddenly with constant headache, intermittent fever and pains in the joints, followed by chills and in a week's time a characteristic multiform erythematous rash (H Vesell and Jos Barsky Am J M Sc 179 589 (May) 1930) The course of the disease extends over several months and meningitis is late, if it occurs at all Of the complications that develop, endocarditis, pericarditis and myocarditis are common Blood cultures are usually negative early in the disease, and later an enriched medium must be used for cultures The spinal fluid is negative except when meningitis develops The only treatment of value is the use of *antimeningococcic serum*.

**MENOPAUSE.**—Changes in the *ovaries*, *thyroid* and *adrenals* enter into the menopause, while the *pituitary gland* is less important In the ovary there is observed an increase in connective tissue stroma formation, at the expense of the epithelial elements, which are compressed by the ingrowth of connective tissue from the periphery to the center This thickening of the tunica albuginea may prevent the rupture of the follicles, causing irregular menstruation Retrogressive changes in the Graafian follicles occur

With the withdrawal of the ovarian hormones, there is much thyroid instability In most cases a temporary hypofunction of the thyroid is noted, in a few a hyperfunction of this gland is observed Clinically, *menopausal hyperthyroidism* manifests itself as a nervous, highly emotional individual, with rapid pulse and loss of weight *Menopausal hypothyroidism* is usually found in patients who show symptoms of myxedema during their active sexual life

In the adrenals a condition of *hyperadrenalinemia* of the medulla usually exists This accounts for the hypertension, vasomotor disturbances, hyperglycemia and glycosuria When the cortex hyperfunctions, there is evidence of secondary masculine sex characteristics such as changes in the voice, distribution of hair, and loss of femininity

C F Fluhman (Am J Obst and Gynec 20 1 (July) 1930) and, independently, C Mazer and J Hoffman (J A M A 96 19 (Jan) 1931) have demonstrated an excess of anterior *pituitary* sex hormone in the blood of nearly 40 per cent of women in the menopause Tandler and Grosz, as early as 1908, called attention to the gross hypertrophy and histologic changes of the anterior pituitary gland following castration

Engle and Evans demonstrated that the anterior pituitary gland of castrated animals yielded more hormone than before castration, all pointing to a compensatory hyperfunction of the anterior pituitary gland in the climacterium

**POSTMENOPAUSAL BLEEDING.**—R W Te Linde (South Med J 23 571 (July) 1930) has analyzed 179 cases of postmenopausal bleeding from the gynecological division of the Johns Hopkins Hospital In 60 per cent of these patients a malignancy of the genitalia was discovered, whereas 40 per cent revealed a relatively benign condition The most common site of the malignant growth was the uterus (55.9 per cent)

Where inspection of the vagina and cervix, or curettage of the uterus do not explain the bleeding, the probability of neoplasm of the ovary should be borne in mind If no evidence of such involvement is obtained at the time of curettage, the patient should be examined

frequently Any increase in the size of an ovary calls for an immediate abdominal section If several years after the menopause, curettage reveals hyperplasia of the endometrium, there may exist a follicular oophoroma or a granulosa cell tumor of the ovary and the patient is to be carefully watched for any ovarian enlargement

**MENORRHAGIA.** — Most cases of menorrhagia are due to a lack of balance between the 2 hormones of the ovary, with a relative increase in the follicle hormone and an absence or deficiency of the corpus luteum hormone, according to W P Graves (*Am J Obst and Gynec* 20 518 (Oct) 1930) This is usually due to ovarian hypofunction, which may be primary or secondary to the pituitary or thyroid hypofunction The endometrium, in these cases, shows hyperplasia, characterized by a "swiss cheese" pattern of the glands, and by dense stroma There is usually a subthreshold quantity of female sex hormone in the blood A similar picture is found in cases of benign menopausal bleeding Recently, stimulating, irradiating doses to the ovaries and the pituitary glands, have seemed to cause considerable improvement The administration of anterior pituitary sex hormone (prolan, fol-lutein) has a tendency to complete luteinization and is, therefore, a logical form of treatment for the patient under 40 years of age In women approaching the menopause, however, who show a compensatory hyperfunction of the anterior pituitary lobe in an attempt to stimulate the declining ovaries, the administration of this hormone is theoretically useless Recent advances in endocrinology have definitely aided in the treatment of this condition.

**MENSTRUATION. — PHYSIOLOGY.**—C G Hartman, W M Firor and E M K Gehrig (*Am J Physiol* 95 662 (Dec) 1930) at the Johns Hopkins Medical School now venture the assertion that there is something radically wrong with the prevailing or "modern" gynecologic theory of the menstrual process, which presupposes ovulation and makes the degeneration of the corpus luteum responsible for the uterine bleeding They have postulated that the cause of menstruation is an active one and have searched outside the ovaries for the source of the stimulus, probably hormonal in nature Working with female monkeys, they have found, as others had observed, that injection of the Allen-Doisy hormone preparation causes bleeding in the animals, whether normal or castrated The effect is however not a direct one, for hypophysectomy abolishes the effect But bleeding occurs in hypophysectomized as well as normal animals by injection of anterior lobe extract or by implants of the fresh gland This is interpreted as a direct effect Furthermore, bleeding from the uterine mucosa is a phenomenon independent of hyperplasia, swelling, or even congestion of the tissues These investigators point out that it does not follow, of course, that bleeding is normally an independent phenomenon

The interactions of the endocrines in particular must be borne in mind Thus, normally in women the follicle stimulating and the luteinizing hormones come into play, ovulation occurs, the anterior lobe is stimulated, and bleeding occurs from a "prepared" or pregravid endometrium of the Hitschmann and Adler type But the stimuli coming from the ovary (or other link in the endocrine

chain) may be insufficient to liberate the first two, but quite adequate to liberate the hormone causing bleeding. If all these hormones are absent, amenorrhea results.

The possible absence of ovulation during long periods in which uterine bleeding may proceed seems now to be established. Hartman, Firoi and Geiling allege that a physiologic basis of uterine bleeding is for the first time demonstrated and the menstruation problem is lifted from the realm of theory and conjecture. It would seem, from the experiments on the monkey, to be possible to produce bleeding in a woman much more readily than stimulating a refractory ovary, and hence a dormant uterus, into action.

**MENSTRUAL BLOOD, MORPHOLOGY OF.**—S H Geist (Am J Obst. and Gynec 22 532 (Oct) 1931) points out that the normal menstrual discharge contains definite morphologic elements whose recognition permits of its differentiation from other hemorrhagic vaginal discharges. In the menstrual blood there is noted a desquamation of the uterine mucosa which is most marked on the second day of the period. In 90 per cent of the patients Geist found either a strip of surface epithelium or larger fragments containing glands and stroma. This may be of value in eliminating the possibility of an ectopic pregnancy in which typical uterine desquamation is absent.

**MENSTRUAL DISORDERS.**—*Treatment.*—Radium in the treatment of *excessive menstruation* in young women was investigated by H A Kelly (J A M A 97 760 (Sept 12) 1931) in 30 patients from 13 to 25 years of age. Of these, 16 patients had an immediate cure with normal periods and 5

patients had a temporary amenorrhea with a later return of normal menstruation. In 6 patients menstruation ceased entirely.

Menstrual hemorrhage in patients under 40 calls for careful investigation with elimination of the cause. If no other cause is discoverable, one or more **curettages** often help. **Radium** and **x-rays** are a last resort, used in small dosage to avoid an artificial menopause.

*Menopausal Hemorrhages*—Here **radium** and **x-rays** find their most brilliant field. Following uterine **curettage**, the patient is given from 1200 to 1500 millicurie hours *in utero* for an hour with instant relief.

In the *hemorrhages complicating fibroid tumors*, Kelly places **radium** first on the list, far ahead of surgery. Following an intrauterine treatment with radium, associated perhaps at once with ray therapy through the abdominal walls, most fibroids shrink in a few months.

*Dysmenorrhea*—In extreme cases not responding to hygienic treatment medical therapy and cervical dilatation, Kelly uses one-sixth erythema dose of **x-rays**, front and back of the pelvis, or **radium**, not over 150 millicurie hours, within the uterus, with variable results.

**MESENTERY. —THROMBOSIS OF SUPERIOR MESENTERIC VEIN.**—J Wulsten (Zentralbl f Chir 56 3155 (Dec 14) 1929) who records an illustrative case, states that a study of the literature since 1860 shows that, owing to the severity of the disease, recovery from mesenteric thrombosis after operation is very rare, only 1 example, published by Doerfler in 1923, having hitherto been recorded of recovery after total resection of the small intestine. Reich, in 1913, collected



250 cases of mesenteric thrombosis which had been published since 1890. Of 214 cases, 100 (47 per cent) were caused by arterial occlusion, and 114 (53 per cent) by venous occlusion. Arteriosclerosis was almost always the primary disease. Autochthonous occlusion was rarer than embolic. The causes alleged were cirrhosis of the liver, alcoholism, and obesity. Thrombophlebitis of the lower extremities was frequently present. The intestinal lesion was usually a hemorrhagic, and less frequently an anemic, infarct. In venous occlusion more serohemorrhagic exudation is found in the abdomen than in the case of arterial occlusion. Most of the infarcts (199 cases) have been found in the superior mesenteric vessels, as compared with only 9 in the inferior. In 10 cases both superior and inferior mesenteric vessels were occluded. All the cases of venous thrombosis were aseptic. Of 91 patients operated on in Reich's series 75 died, including 43 in whom peritonitis was already present or developed subsequently. During the last 16 years cases of mesenteric thrombosis have been recorded by W. Wolff (1919), Brutt (4 cases in 1922), Doerfler (1923), Bruns (1924), Klein (24 cases in 1926), and Petermann (1926). Wulsten's patient was a man aged 64, the subject of alcoholism and varicose veins, in whom the diagnosis of mesenteric thrombosis was made before operation; 11 feet of the small intestine which showed typical hemorrhagic infarction were resected. The superior mesenteric vein and its finest branches were found to be completely thrombosed. Recovery ensued.

**CYSTIC TUMORS.**—On the basis of statistically collected cases of mesenteric cysts, F. Becker (Schweiz med

Wehnschr. 59, 979, Sept. 28, 1929) reports that such cysts have been observed considerably more frequently in recent years, evidently as the result of more frequent operative interventions, but are still a rare finding. Because of the greater length of the mesentery of the small intestine, the absolute number of cysts is greater in this portion of the mesentery, but to 1 meter of the mesocolon there are 10 cysts, whereas to 1 meter of the mesentery of the small intestine there are only 7 cysts. The distribution is about the same in the different portions of the mesocolon.

The symptoms are too varied to be of much aid alone in the diagnosis, and the clinical examination often discloses only the presence of a tumor without revealing its nature. Therefore, the diagnosis can be only suspected in most of the cases. The prognosis in cases operated upon is by no means favorable, the mortality ranging from 22 to 31 per cent and in acute cases sometimes being as high as 52 per cent.

With regard to the various methods of *treatment* the author says that puncture not only fails to give a permanent result, but is associated with the danger of injury of the intestine and peritonitis and, in cases of echinococcus disease, with metastasis. Marsupialization gives good end-results, but is associated with a protracted and not always uncomplicated course and also with the danger of peritonitis. By far the best form of treatment is **enucleation** which is the cleanest and quickest procedure, but is applicable in only from 30 to 40 per cent of the cases. In the others there remains only **resection** of the cyst usually with involved portion of the intestine, an operation which is contraindicated when the general condition is poor.

For *inoperable* cases the treatment is **puncture** and **radium** irradiation

The author reports a case personally observed, with a successful removal of a lymphangiomatous mesenteric cyst with signs of inflammation

**METABOLISM.—BASAL METABOLISM.**—With the increased ease of basal metabolism determinations, they have become an almost routine procedure in a complete examination. It is well to remember that their value as a diagnostic aid and an indication for therapy is proportional to an appreciation of all the factors that influence the energy exchange of the body

A timely article by C. A. McKinlay (Minn. Med. 14:713 (Aug. 1931)) points out the fact that a decreased metabolic reading may be obtained in other conditions than true hypothyroidism. He stresses the fact, which has also been brought out by other writers, that occasionally an apparently normal individual may have a reading below the accepted "low normal" of minus 10. He also points out the possibility that other glandular abnormalities than those of thyroid origin may give a lowered reading, but these are all more or less easily recognized clinical entities. In addition, starvation frequently gives a low metabolic rate. This reduction is probably due to a protective mechanism on the part of the body, not, however, a primary thyroid influence. While starvation is rare, the physician frequently sees cases of undernourished individuals who, for various reasons, have restricted their diet to the point of caloric deficiency. Although in undernutrition thyroid deficiency is not primarily present, if the condition be of long standing there may be secondary alteration of thyroid function and the

use of thyroid has been of help as an adjunct in the treatment of these cases

Since muscular inactivity tends to depress the basal metabolism, it should be remembered that in invalidism, as in certain anemias and arthritic conditions with long periods of inactivity, there may exist secondary lowering of basal metabolism

Keeping in mind, then, that physiologic and pathologic states, other than a primary change of thyroid function, tend to depress the basal metabolism of the body, the physician will be in a position to evaluate a reduced basal metabolism in individuals without myxedema. It presupposes that a complete study of the case has been made, that chronic infection, including tuberculosis, and anemias or other chronic states with invalidism, have been excluded or evaluated and that there is no demonstrable cause of symptoms. After exercising such caution, there remains a group of cases with fatigue, exhaustion, low energy level, anemia, unexplained dizziness, sensitivity to cold, drowsiness, obesity without overeating, sterility and menstrual disorders, in which the therapeutic trial of thyroid extract is justified even though physical signs in the form of skin and hair changes are minimal or not demonstrable. While a number of these individuals may respond well to treatment, there will be differentiated by this therapeutic test the group without improvement and presumably without any thyroid deficiency. This group is worthy of further study. Undoubtedly some of them have a nutritional deficit sometimes on an infectious basis which has not been evaluated. Although undernutrition itself tends to depress basal metabolism, it is somewhat paradoxical that undernutrition may be, and often is, due in some degree to the high

rate of energy exchange characteristic of hyperthyroidism. In obesity, normal values usually obtain, although there is a tendency for some individual cases to have low basal metabolism.

Some of the group with low basal metabolism appear to be entirely normal. Is their low metabolism comparable to the physiologic slow pulse, low temperature and low blood-pressure of certain individuals? In such individuals studied after the development of some complaint, the normality of a low basal rate for the individual should be kept in mind. Whether some of this group will later develop hypothyroidism or myxedema is a question. Against this, evidence exists that hyperthyroidism is a precursor of myxedema in a certain percentage of cases where hyperfunction of the gland leads later to retarded or absent activity.

A study has been made of a group of individuals without marked physical defects. Determination of the basal metabolic rate was made often on account of rather minor noncapacitating disturbances of function, as overweight, underweight, menstrual disturbances and fatigue, and also on account of colloid goiter. None had myxedema. Multiple determinations made on a group of 155 students, aged 17 to 35, at the University of Minnesota, are referred to. The Roth-Benedict apparatus was used in 134, the McKesson in 20, usual standard basal conditions were obtained and Aud-DuBois standards were used.

It was found that over one-fourth of this group had low basal metabolic rates. While in some of these underfunction of the thyroid may be present, as indicated by response to substitution therapy, in many others no such underfunction was established. A study is being made of this group in order that

the proportion of normal individuals may be established from the results of complete routine examination.

In conclusion, the increased clinical use of the determination of basal metabolism makes imperative a critical attitude in its interpretation as a diagnostic aid. It must be kept in mind that undernutrition and inactivity tend to depress the basal metabolism and that certain apparently normal individuals have a basal metabolism below normal limits according to standards and procedure in common clinical use. The findings in a group of 155 young adults with good working capacity show that in 27.0 per cent the basal metabolic rates were below normal.

[Many of these cases with lowered rates and failure of response to thyroid therapy have been found by Lahey and others to have a normal blood cholesterol, while in the cases which responded clinically to thyroid extract the cholesterol readings were found to be above normal.—Ed.]

**Effect of Physical Training on Metabolism.**—The value of physical training is thought to be due to its influence in increasing the metabolism of the tissues. Some investigators have felt that the changes in the heart, circulatory, and respiratory mechanisms were the most important factors in the adjustment brought on by physical training. Efforts to interpret from laboratory findings the greater efficiency of the trained athlete over the untrained individual have been disappointing. E. C. Schneider and A. O. Foster (*Am. J. Physiol.* 98:595 (Nov.) 1931) report the results of their observations on students of Wesleyan University. The muscle cells present themselves as a very important center in this study. If their characteristic exchange of energy is

altered, it should exhibit itself in a change in the basal metabolism. Recognizing that metabolism is a cellular process and that each living cell uses its share of the total oxygen absorbed by the individual, the real problem is to determine whether or not the cellular processes of the body are accelerated, retarded, or unaltered by physical training.

It is obvious that if the cells are stimulated to greater activity, they will use more oxygen, but if their life processes become more efficient, they will use less oxygen. Schneider points out that there is a widespread belief that the body is physically and mentally more efficient if regular exercise is taken. While it cannot be assumed that cellular metabolism becomes more efficient during training, it would seem that this might be a very logical explanation for the fall in basal metabolic rate observed in athletes and nonathletes while under a regular course of athletic training.

The authors have shown that all men do not respond in the same manner to a period of training. Of 7 nonathletes who were under observation during periods of daily moderate exercise, 3 showed a definite fall in the basal metabolic rate, 2 a rise, and in 2 others no change was noticed. Ten athletes examined also varied in their reaction to their training, 8 showing a drop in their basal metabolic rate, 1 an increase, and another no change whatsoever.

The interpretation of these seemingly conflicting results is offered by the authors as follows: If, as has been mentioned before, the life processes in the muscle cells become more efficient with use, they may require less oxygen and their metabolism will fall. On the other hand, if a period of physical training should at the same time result in an increase of the muscle mass of the body,

it is only natural to suppose that this increased protoplasm would require more oxygen for its metabolism. The authors conclude, therefore, that if during a period of training the gain in cellular efficiency overbalances the gain in the mass of body protoplasm, a fall in the basal metabolic rate will result. If, on the other hand, there occurs a considerable increase in the size of the muscles, due to a formation of active protoplasm, this may overshadow the gain in cellular efficiency and result in an increase in the basal metabolism. And, lastly, if the increase in efficiency should just be counterbalanced by the new production of protoplasm, the basal metabolic rate would be unchanged during the period of physical training.

These results and the conclusion deducted therefrom would seem to explain the many conflicting reports of the basal metabolism changes during physical training.

#### MINERAL REQUIREMENT.—

Mineral metabolism is gaining in favor. There is evidence that the interrelation of minerals is more important than the actual amount of a given one. The results on the regeneration of hemoglobin, when iron is supplemented with copper, or those in bone structure if there is a continued disturbance in the calcium and phosphorous ratio, bear out this statement. The storage of these elements in the body is not in an appreciable amount. This varies with the individual, thus, protection against deficiency depends upon a liberal supply and utilization of foods of high mineral content, particularly calcium, phosphorus, iron, copper and iodine.

*Calcium* and *phosphorus*, which are usually found in a ratio of 1:1, are of joint importance as the calcium is stored as a calcium phosphate. Their utiliza-

tion is largely dependent upon various factors

H B Brown and A T Shohl (J Biol Chem 86 245 (Mar) 1930) indicate that vitamin D controls the calcification of the skeleton by dissolution and deposition of bone salts, providing the calcium and phosphorus are supplied in sufficient amounts and correct ratio. A hormone secreted in the parathyroid apparently controls the concentration of the calcium, as the removal of the gland results in a low blood calcium. The acid and base equilibrium of the body is an influence, as a diet yielding an acid ash will show increased elimination of calcium in the urine.

The work of H C Sherman and L E Booher in the calcium content of the body in relation to food (J Biol Chem 93 93 (Sept) 1931) indicates that in growing rats, the amount of calcium in the body varies with the content of the food, although those on a low calcium intake may have the same physical appearance as those on a high intake, but on chemical analysis, the bodies were shown to be calcium poor.

The malformation and early decay of teeth, which are formed during the latter part of fetal life or infancy, may be traced to a deficiency of calcium and phosphorus in the mother's diet during pregnancy or lactation. Percy Howe, of the Forsythe Dental Clinic, Boston, expresses the opinion that the exclusive use of meats, refined cereals, and sweets is an outstanding fault in diet. All of these are poor in calcium. Clinical and experimental observations indicate that active caries may be an indication of nutritional deficiencies. Vitamins C and D and minerals, calcium and phosphorus, are essential and a diet rich in these is thought to be a vital factor for insuring normal teeth.

The irritability of the nervous system is largely dependent upon the amount of calcium, phosphorus and sodium ions present in tissue and body fluids. A decrease in calcium tends to cause an increased irritability. In the adult, the minimum calcium requirement is 0.67 Gm (11 grains) per day. In the case of a child 0.75 to 1 Gm (12 to 15 grains) provides a more liberal margin of safety for growth and tissue building. Growing boys may require 3 to 4 times more calcium than men. This daily requirement may be adequately met for a child, if a balanced diet is supplemented with a quart of milk, or in the case of an adult, 1 pint may be used. Foods rich in calcium include milk, cheese, carrots, cabbage, turnips, beets, apples, oranges and prunes.

*Copper* holds a unique position in its ability to stimulate hemoglobin formation. This is shown by the work of H. L. Keil and V. E. Nelson on the rôle of copper in hemoglobin regeneration and in reproduction (J Biol Chem 93: 49 (Sept) 1931), where, in the case of rats with nutritional anemia produced by a milk diet, copper when added to the milk, was the only element to produce a positive effect in the hemoglobin. Considerable work has been done to indicate its values for certain infantile and adult anemias. Foods rich in copper include wheat germ, almonds, oats, kidney beans, rye, peas, asparagus, maize, lentils and barley.

The *iodine* content of the body, according to W. Weston (Am J Pub. Health 21:715 (May) 1931) may average 51 mgm in the musculature, 10 mgm in the thyroid, and the remainder in the spleen, suprarenals, salivary glands, bone and skin. The normal requirement is averaged at 0.05 mgm per

day but Weston feels that one-tenth of this amount is sufficient to prevent or cure endemic goiter. The utilization of this element in the system is affected by too high a fat or protein diet.

As inorganic iodine leaves the body quantitatively in a rather short time (less than 24 hours), mostly through the kidneys, the opinion is expressed that organically bound iodine in food-stuffs, which is set free slowly, may be a more efficient and practical method of supplying the mineral. According to Weston, sufficient iodine in the diet furnishes an important element which enables the thyroid gland to synthesize thyrotoxin, whereas a deficiency may result in goiter—this being particularly common in girls and women at adolescence or during pregnancy, when the demands on the body are unusually great. The lack of this element over several generations may result in the birth of feeble-minded children, congenital idiots and myxedema in adults. Foods of high iodine content include sea fish, spinach, lettuce, beans and carrots which are grown in districts where the soil and water are rich in this mineral.

*Manganese* is so prevalent in plant and animal tissue that the opinion is reached that it is necessary for physiological functioning. Some experiments indicate that manganese may have an influence on hemoglobin formation. H. S. Mitchell and L. Miller (J. Biol. Chem. 92:421 (July) 1931) indicate that when manganese was fed to rats as a supplement to iron and combination of iron and copper, it stimulated growth but its reaction on the hemoglobin was negligible.

*Iron*—A survey of 150 American families indicated that the iron intake averaged 14 to 20 mg daily. This is just sufficient to meet the "Sherman

Standard" of 15 mg. During the fetal life and early infancy, iron is found stored in the liver as a safeguard during the nursing period.

Recent work indicates that iron is not the only substance needed to build hemoglobin. M. S. Lewis (J. A. M. A. 96:1135 (Apr. 4) 1931) indicates that iron and copper, given in combination to children with nutritional and secondary anemia, produces more effective results than when iron is given alone. For this reason, foods rich in iron may be more effective in the regeneration of the hemoglobin, as they may contain an additional substance as copper, also active in this work. Foods rich in iron include pork, beef, calves' liver, lima beans, peas, lean beef, steak, spinach, oatmeal, raisins, eggs and green vegetables.

*Aluminum, nickel, silicon and zinc* are constituents of some foods and may be found present in the human organism in varying amounts, but as yet there is little evidence of their nutritional value.

Detrimental results from *mineral deficiencies* may not be noticed as quickly as those of protein or energy producing foods, but if these deficiencies are carried over a period of time, the results may be permanent or more difficult to correct.

**METAPHEN.**—G. W. Raiziss, M. Severac and J. C. Moetsch (J. A. M. A. 94:1199 (Apr. 19) 1930) find that metaphen, in aqueous solutions ranging in strength from 1:500 to 1:2500, completely sterilizes the skin of live rabbits contaminated with broth cultures of *Staphylococcus aureus*, *Streptococcus hemolyticus* and *Bacillus subtilis* after preliminary cleansing. The drug is so powerfully germicidal that 1:20,400,000



dilution is bacteriostatic for *Staphylococcus aureus*

According to E. C. White and J. H. Hill (J. A. M. A. 95:27 (July 5, 1930)), in dilution of 1:500, metaphen is not a reliable disinfectant, and can not be depended upon to sterilize normal human skin after a 5 minute application. They claim that the amount of metaphen carried over on the cotton swab into the culture tubes containing 10 c.c. of broth, as used by Raiziss and his associates, was sufficient to inhibit growth of the organisms from the treated skin in those subculture tubes.

J. A. Kolmer and M. J. Harkins (Arch. Surg. 23:1007 (Dec.) 1931) repeated the experiments of Raiziss and his associates, with the contradictory findings of White and Hill in mind, and their observations also indicated that it was necessary to make subcultures in 100 c.c. or larger volumes of broth, in tests of the bacterial activity of metaphen.

The amount of metaphen carried over into the subcultures of 10 c.c. of broth on the cotton swabs was not enough to inhibit growth when 4 mm. loopfuls of a 24-hour broth culture of *Staphylococcus aureus* was added thereto, for after 72 hours of incubation, subcultures so treated showed heavy growth, but the amount of metaphen so carried over might be, and apparently was, sufficient to be bacteriostatic to the same varieties of organisms after they had been reduced in their virility by the application to them of 1:500 solution of metaphen for 5 minutes.

Tests of the efficiency of metaphen, in 1:500 dilution, as a disinfectant of human skin, indicate that the condition of the skin of the individual and the amount of bacterial contamination are factors which influence the findings.

Tests of 20 human volunteers whose skin on the forearm was treated with 1:500 metaphen solution and then cultured, those who were engaged in dirty work, such as cleaning, showed heavier growths than technicians and staff members.

The bacterial flora of the skin varies in different depths of the skin. Therefore, it is not a fair test of the skin disinfecting powers of an antiseptic, to first prepare the skin by scrubbing with soap and water, followed by the application of alcohol and ether, and then contaminating the skin surface with broth cultures of bacteria, such technique results in most of the bacteria being on the surface of the skin, and not located at varying depths, and so will yield more favorable results upon application of the antiseptic than would be found if untreated skin were tested. However, the application of 1:500 aqueous solution of metaphen to unprepared skins for 5 minutes resulted in the complete destruction of staphylococci in 95 per cent of cases. The staphylococci are the most important organisms to destroy, from the surgical standpoint.

**MYCOLOGY.**—Bacteria in medicine are normally parasitic, while fungi are normally saprophytic and only at times invade man. When these latter actually adapt themselves to man they become formidable parasites as trichophyton, microsporon and achorion.

The importance of mycology to tropical medicine is evidenced by the fact that a survey of 700 dermatological cases in Porto Rico led to the belief that one-third to one-half of all skin diseases seen there in clinics were of mycotic origin. With the exception of tropical sprue, these diseases are infrequent

causes of death or serious sickness. (B K Ashford: Arch Dermat and Syph 22 1 (July) 1930)

**MYOMECTOMY.**—At the Congress of Obstetrics and Gynecology held at Rome, February, 1931 (J A M A. 96.1811 (May 23) 1931), Baciali, of Novara, presented the official paper on myomectomy. To classify under the same term myomectomy the simple removal of a pedicled fibroma and the enucleation of one or more interstitial nodules has brought forth confusing statistics. With regard to the technic of enucleation, the author advocates chiefly, suturing of the peritoneal flap according to the method of Pestalozza, omental grafts, preventive hemostasis and abdominal and vaginal drainage.

Among the *contraindications* to myomectomy, the state of conservation and consistency of the tumor should be considered. The modern methods of hysteroscopy and hystero-graphy may show the extent and location of the fibromatous nuclei with reference to the uterine cavity and tubal openings. The normal resumption of menstrual function, the possibility of future pregnancy and of recurrences should be borne in mind.

Recurrences range from 5 to 15 years after operation. In pregnancy, simple myomectomy performed early may give good results, whereas enucleation still presents considerable danger.

**INDICATION.**—V Bonney (Lancet 1:171 (Jan. 24) 1931) claims that although *fibroids* may often be managed conservatively, myomectomy is not always the operation of choice, as sometimes it is much more difficult than a corresponding hysterectomy. For women over 41 years of age it is to be preferred to hysterectomy only when it is definitely the lesser operation or when the

patient demands it. For women of 41 or under it is the operation of choice. Myomectomy should not be performed unless the remainder of the uterus is healthy and there is no suspicion of malignancy.

The various forms of nonmalignant degeneration such as "red," myomatoid, hyaline, cystic nevoid, do not contraindicate conservatism. Bonney has enucleated such fibroids on many occasions with impunity.

For the past 18 years Bonney has performed the operation 403 times, 237 of the tumors being multiple. A tumor on the lateral wall is more troublesome to remove than one on the anterior wall and a posterior wall tumor is most difficult of all. His operative mortality was 1.7 per cent.

He believes that the tendency to the formation of fibroids is a passing phase in the uterine tissues, since recurrences are quite rare. The nuclei of all the future fibroids are laid down by the age of 30. Before this period there is greater chance of recurrence. Among 77 patients in whom pregnancy was desired, 30 or 39 per cent. conceived after myomectomy.

**TECHNIC.**—In his technic a clamp is applied to the lower uterine body which compresses both uterine arteries at the same time. By this means, together with the application of ring forceps on each ovarian artery, all 4 main vessels are temporarily controlled, so that the field of operation will be practically bloodless. The uterine clamp is applied from the pubic end of the abdominal incision, and it is essential that the round ligaments should be included in its grip, otherwise the tightening causes it to slip down on the conical cervix until, finally, it is compressing the

vagina below the uterine arteries. The clamp and forceps are not removed until the suturing of the uterus is completed. When they are taken off there is a certain amount of oozing from the suture holes, which soon ceases after the uterus is returned to its place. Tumors not directly accessible through the median anterior incision are reached by secondary incisions made from the primary incision. In the majority of cases, Bonney advises opening and exploring the uterine cavity in order not to overlook a small submucous myoma or polyps, and thus, perhaps, leave behind the chief cause of the menorrhagia for which the operation is being performed. The opening of the uterine cavity will not increase the risk of the operation unless the uterus is already infected, in which event myomectomy should never be attempted. [A preliminary curettage of the uterus is a much safer diagnostic procedure—Ed.]

**MYXEDEMA.**—Thyroid therapy dates back as far as 1891, according to G. R. Murray (Brit. M. J. 2:1030 (Nov. 30) 1929). He reports 3 cases of spontaneous recovery of cases of myxedema following thyroid therapy as previously reported by Hun and Prudden, Garrett Anderson and Fraser, of Paisley. These cases were recorded 2 years after Murray's case and explained by him as the basis of either a temporary disablement of the thyroid with recovery of function after the administration of thyroid extract or an accessory gland hypertrophied sufficiently to compensate for the atrophy of the thyroid gland already present.

**PATHOLOGY.**—The significant histologic changes in myxedema are summarized by M. J. Reuter (Arch. Dermat. and Syph. 24:55 (July) 1931)

as follows: hyperkeratosis of the epidermis with hyperkeratotic plugging of the hair follicles and sweat ducts, irregular scattered atrophy of the epidermis with degenerative changes in the epidermal cells, pronounced edematous changes in the corium and, in consequence, a spreading apart of the collagen and elastic fibers associated with mild degenerative changes, a sparse cellular infiltrate about the vessels in the upper part of the cutis and in a few cases about the hair follicles and sweat glands, and the constant presence of a mucinous staining material in considerable quantities. The author believes the characteristic appearance of myxedematous individuals is due to the edema plus the excess of mucin in the corium. The information regarding mucin in the tissues is rather meager at the present time and it may not be taken as a diagnostic finding in myxedema.

**ETIOLOGY.**—The development of myxedema occasionally during the administration of iodine to patients who have a normal basal metabolic rate following subtotal thyroidectomy for exophthalmic goiter is discussed by W. O. Thompson, P. K. Thompson, A. G. Brailey and Cohen (Am. J. M. Sc. 179:733 (June) 1930) who believe it is due to an inhibition of the normal secretion of the thyroid extract. In the same way he states that it is possible for iodine to cause a reduction in the high basal metabolic rate of exophthalmic goiter.

**COMPLICATIONS.**—In reviewing the cases of myxedema with *mental symptoms* previously reported, to which he adds 3 personal cases, L. H. Ziegler (J. Neurol. and Psychopath. 11:20 (July) 1930) believes that the thyroid deficiency brings about a physiological depression which may precede abnormal

mental states. He also considers that the latter conform more or less to the personality reaction of the individual patient, rather than follow any fixed clinical picture of mental disease. All his patients improved on administration of desiccated **thyroid gland**.

E. Ruds (Hospitalsted 73 25 (Jan

2) 1930) reports a case of myxedema in a male, aged 69 years, believed to be of arteriosclerotic origin. X-ray examination revealed calcification of the superior thyroid artery. The marked cerebellar symptoms, asynergy, dysmetria, ataxia and adiadochokinesis yield to treatment with **thyroidin**.

## N

### NARCOTICS.—IN OBSTETRICS AND GYNECOLOGY.—

An attempt is being made by a united group representing the American Medical Association, the Committee on Drug Addiction of the Division of Medical Sciences of the National Research Council, and the Division of Mental Hygiene of the United States Public Health Service, to reduce the legitimate use of addiction drugs to a minimum. Narcotics, however, still remain indispensable to the obstetrician. J. B. DeLee (J. A. M. A. 96 1007 (Mar 28) 1931), discussing their use in obstetrics, states that the **prevention of abortion** is the most common indication for narcotics during pregnancy. *Morphine* has saved numerous pregnancies and is more effective than chloral or bromides.

For **pernicious nausea and vomiting**, *morphine* or *cocaine* are occasionally used to stop vomiting, while *tincture of opium* is often added to allay rectal spasm and aid retention.

Pregnancy does not contraindicate the use of narcotics, as the child does not suffer except from an overdosage that would endanger the mother.

**Eclampsia** is perhaps the most important indication for *morphine* although it is often combined with *sodium amytal*, *magnesium sulphate*, *chloral* and *bromides*.

In **placenta previa**, while preparations for stopping the hemorrhage are being made, *morphine* will calm the uterus, reduce the bleeding and quiet the apprehensiveness of the patient. This is equally true in cases of **premature separation**.

During labor *opium* derivatives are indispensable as chloral, barbituric acid compounds and other substitutes are ineffective.

Whereas the routine administration of narcotics in labor causes numerous fetal deaths, no one can deny that the scientific administration of narcotics at this period is warranted both for relief to the mother and because, by moderating the force of the uterine contractions, they may relieve the baby from injurious pressure and preserve its life and integrity. By preserving the mother's strength in a prolonged first stage, narcotics actually shorten the second stage.

For the **restlessness following a severe postpartum hemorrhage**, *morphine* is quite valuable, as well as for cases of **retained placenta** to reduce muscular spasm.

In the puerperium narcotics are less essential. After-pains seldom need more than the barbituric acid preparations. *Morphine*, however, is highly useful for the **insomnia of puerperal infection** and for the **septic diarrheas**.

In the practice of **gynecology** *morphine* is similarly required. Cocaine is seldom employed but *procaine hydrochloride* has extensive use. Most gynecological operations can be done under local anesthesia with morphine. For the **postoperative pain** and abdominal symptoms *morphine* is indispensable. To bind up the bowels after **pelvic plastic surgery** *opium* derivatives are necessary.

For the chronic gynecological diseases, however, such as fibroids and carcinoma, morphine had best be omitted. For the woman suffering the **pains of incurable cancer** *morphine* is the gynecologist's sheet anchor.

**NEMBUTAL.** See ANESTHESIA, BASAL.

**NEPHRITIS.—ETIOLOGY.**—Experimental work on the production of an *acute nephritis* by means of a pneumococcal autolysate by J H Brown, S S Blackman and G Rake (Bull Johns Hopkins Hosp 48 74 (Feb) 1931) has been the result of years of intensive observation of the subject by many students. The authors found that in their human autopsy records of about 40 to 50 per cent of those dying from *pneumococcal infection*, the lesions found in the kidneys often parallel those observed and produced in rabbits. In order to rule out the possibility of a toxin from the autolysate coming from the action of the disintegrating bacteria upon the broth rather than an actual endotoxin, experiments were carried out in which the pneumococcus was allowed to autolyze in normal saline. This autolysate produced a skin reaction in rabbits and kidney lesions resembling in every way those obtained after injection of the broth autolysate. The dosage varied from 0.3 to 2.4 c c with 1 to 9

injections. Most of the rabbits showed pathologic changes in the kidneys, with involvement of both the glomeruli and the tubules. The kidneys were swollen, edematous and of a pale yellow color, with petechial hemorrhages on the surface. Microscopically, the glomerular capillaries showed hyaline and fibrin thrombi, blood and fibrin in the tubules, and a necrosis of the epithelial glomeruli and tubules. The conclusion drawn by the authors is that the average clinician does not always look for or consider nephritis as a complication of pneumonia, but they have certainly proven its possibility experimentally.

O Romcke (Nordsk Med Tidskrift 344 (May 29) 1931) reports a series of cases of *acute and chronic nephritis* which he believes were markedly benefited by the removal of *tooth infection* and for this reason considers it as an etiological factor.

In 1 case an outbreak of eczema was followed by a pustular dermatitis which developed coincidently with the appearance of blood in the urine. The patient also suffered from a bilateral otitis media and when operative intervention was taken, the albuminuria and hematuria which had persisted for 8 months cleared up in 3 weeks. Another case which he reported was an individual with pulmonary tuberculosis plus a definite nephritis, which disappeared with the removal of an infected tooth.

H Kutschera-Aichbergen (Ztschr f klin Med 117 233 (June 22) 1931) believes that *chronic nephritis* develops nearly always from that form of acute nephritis which begins with hypertension. Neither the development nor the malignant course of the nephritis of chronic hypertension can be explained by a persistence of those external fac-

tois that originally cause the acute disease. He believes that vascular changes are of primary importance in the development of a chronic phase of the disease. To him, then, the chronic hypertensive nephritis and likewise the acute form should, therefore, not be classed with the inflammatory, but rather with the vascular renal changes. In contradistinction to the so-called essential hypertension, in which the tonus regulation of the arteries is disturbed, there is in the beginning stage of this disease primarily a disturbance in the vascular motility. The outcome of the vascular disease is the same in both cases, *i e*, arteriosclerosis.

**DIAGNOSIS.**—The importance of the recognition of the presence of acute circulatory decompensation in the diagnosis and treatment of *acute diffuse glomerulonephritis* is stressed by R. J. Levy (Am Heart J 5 277 (Feb) 1930), because the cardinal symptoms, as shown by nitrogen retention in the blood, may be absent. Ten cases of this description are reported by the author. The only clue to the diagnosis is obtained by a proper interpretation of the circulatory symptoms. The sudden advent of circulatory decompensation should lead the physician to suspect the presence of acute nephritis. Although it is generally believed that the edema in acute diffuse glomerulonephritis is a "tissue disturbance" caused by a derangement of metabolism, the fact must not be overlooked that water retention may also be due to a circulatory disturbance. A decision and a proper one in this instance is imperative as a guide to the proper therapy.

**TREATMENT.**—A. A. Osman (Lancet 2.945 (Nov 1) 1930) summarizes the results of the use of alkalis in the treatment of *chronic nephritis*

during the past 7 years. He believes they may be used either for their prophylactic or therapeutic benefit. In the 40 cases which he reports all the individuals had symptoms severe enough to place them in bed at least 3 months before treatment was instituted. Most of the cases had been previously treated by the usual sweating, purgation, salt depletion, urea, high protein diets, thyroid extract, purine diuretics or decapsulation without benefit. The mortality under the alkaline treatment in 5 years was 37 per cent. According to the author, the chief value of alkalis is in the promotion of diuresis and thus ridding the tissue of excessive water or edema. Therefore, the cases which are most suitable for this therapy are the chronic ones in which there is a large amount of edema with oliguria. In many instances, the administration of **potassium citrate** and **sodium bicarbonate** raise the blood bicarbonate to a point where diuresis will be induced and free the system of all edema. In the series reported it was possible in 80 per cent to obtain complete and lasting control over the edema, and the average period occupied by the treatment was from 6 to 8 weeks.

**Diathermy** is recommended by H. Eppinger (Klin Wchnschr 9 2043 (Nov 1) 1930) for the treatment of *acute nephritis*, 3 cases being reported in which there was vascular tension and in some instances it proved beneficial. A lead electrode was applied to the renal region and an indifferent electrode to the abdomen. The intensity of the current was from 1.5 to 3 amperes. Each treatment lasted 2 hours and they were given twice a day. In conclusion, the author believes that diathermy should be given a trial in all cases, although it may not prove 100 per cent satisfactory.



H O Mosenthal and B Ashe (Am J M Sc 180 476 (Oct) 1930) discuss the use of **blood transfusions** in cases of *Bright's disease*. They consider the fear of many clinicians to use such a measure is a preconceived idea and not the result of clinical experience. They believe from their own observation that anuria following transfusion is rare, but in many instances a nephritis with anuria was improved thereby. A pronounced diuretic effect was noted from the transfusion of blood. The writers distinctly state that transfusion in Bright's disease does not raise the blood-pressure, injure the kidneys, nor relieve or aggravate uremic symptoms. They consider that the chief function of transfusion is in the relief of the progressive anemia accompanying impairment of renal function. In many instances it is necessary to repeat the transfusions if there is considerable damage to the renal parenchyma.

W Lemberger (Med Klin 26 308 (Feb 28) 1930) asserts that in *acute nephritis* there always exist circulatory disorders, particularly a marked increase in the arterial pressure. He believes the counteraction of this feature is best accomplished by **cardiotonic therapy**, by **absolute abstinence from fluid intake** and by **venesection**.

In many instances, the author believes that edema is a defense reaction of the tissues and body to eliminate vasotoxic substances from the vascular system. If this is absent, there is a marked rise in vascular tension and in some instances where venesection was performed, he attempted an internal drainage of the vascular system by changing the osmotic pressure conditions.

He gave a subcutaneous injection of 0.75 mgm. of **histamine**. By means of a self-retaining stomach tube,

the gastric juice was withdrawn. By this method Lemberger reasoned that under the influence of histamine the chlorine contents of the blood and urine decrease in proportion. Histamine also enhances the permeability of the capillaries and this, together with an increased osmotic pressure between the blood and tissue fluid, results in a draining of the blood serum into the tissues. The author points out that histamine affects the glands of the stomach directly and not through an influence upon the vagus nerve. He also states that it does not weaken the heart but causes a peripheral vascular dilatation.

**Diet.**—The significance of uncooked food in the dietetic treatment of nephritis is discussed by K Eimer and W Voigt (Ztschr. klin f Med 113 224 (May 23) 1930). By their methods, the patients are not so carefully restricted and the results have been favorable. In *subacute* and *chronic nephritis* a diet of uncooked food causes a liberation of large quantities of water from the organism and this is beneficial. There is a decided improvement in the height of the blood-pressure and the patients feel much better symptomatically. They believe that in the preuremic state of chronic nephritis, better results are obtained with this form of diet than with any other.

A comparison may be made between the *nephritic* and the *optimum diet* in regard to the nutritional adequacy under the essential headings of Calories, Vitamines, Residue, Water, Mineral Salts and Protein.

**Calories.**—Twenty-two hundred to 3000 calories may constitute the average caloric requirement of the optimum diet, but the nephritic, as the diabetic, if kept about 10 per cent underweight and maintained on a subcalorie diet, does

better as he is not called upon to metabolize foods, other than those strictly needed

McLester ("Nutrition and Diet in Health and Disease," 1931) expresses the opinion that the effort to preserve the full caloric value of the nephritic diet with a large fat quota is a mistake, for the diet high in fat does not allow economical utilization of protein. Thus, sufficient calories to prevent loss of weight (except in the case of obesity) and to preserve a reasonable amount of body fat, is proper for protein economy.

The total caloric intake may approximately average 2000 calories, with the carbohydrates as the chief form of energy. In cases where obesity is a factor for consideration, a gradual reduction in weight of 1 to 2 pounds a week may be accomplished by restricting the calories to 1000 or 1500 per day per person.

**Vitamines.**—Fortunately, the optimum and nephritic diets compare favorably in vitamine A, B complex, C, D, and E content, which is essential for growth, reproduction and maintaining health.

Such foods as

Butter, milk, vegetables, and eggs will provide vitamine A

Vegetables, cereals, meat, yeast will provide vitamine B

Citrous fruits and vegetables will provide vitamine C

Egg yolk, cod-liver oil will provide vitamine D

Milk, lettuce, wheat germ will provide vitamine E

The majority of these foods can be adequately included in both diets.

**Residue.**—Both diets have a moderately high residue, owing to the abundance of fruits and vegetables predominating.

**Water.**—Eight to 10 glasses of water is the usual requirement of the *optimum diet*, approximately  $2\frac{1}{2}$  liters (quarts). In the *nephritic diet*, extremes in either direction should be avoided and the intake of water limited to an amount which will balance the output.

McLester (*loc cit*) states that an adequate water supply may be adjusted to the kidney impairment and that restriction of the total fluids below a liter (quart) is seldom necessary and rarely should exceed 2 liters (quarts). Thus, from 1 to  $1\frac{1}{2}$  liters, or 1500 cc (3 pints) a day, is advisable if no acute condition prevails.

**Mineral Salts.**—An unrestricted sodium chloride content in the *optimum diet* may average 5 to 10 Gm ( $1\frac{1}{4}$  to  $2\frac{1}{2}$  drams) daily, whereas, in the case of the *nephritic diet*, it is essential to have a lower content, as an excess of salt only adds to the work of the kidney. There are various degrees of salt restriction.

The salt-poor diet includes foods which are slightly salted while being cooked, but no additional salt is added at the table. In this case, the sodium chloride may average 2 to 4 Gm ( $\frac{1}{2}$  to 1 dram) daily, which is usually sufficient limitation and the food is palatable. In the cases where edema is present, a salt-free diet is advisable in which foods are cooked and served without salt. The natural salt content of this diet averages 0.5 to 1 Gm ( $7\frac{1}{2}$  to 15 grains) daily.

The adequate requirement of mineral salts such as calcium, phosphorus, iron and iodine in the *optimum diet* is as follows:

Calcium	0.68
Phosphorus	1.32
Iron	0.015
Iodine	Traces
(Sherman "Chemistry of Food and Nutrition")	

A Committee studying the nutritional quality of nephritic diets reported at the American Dietetic Convention in October, 1931, that the mineral content depends upon the protein allowance. It was found that

1 Diets with less than 40 Gm (10 drams) of protein cannot supply an adequate mineral quota

2 Diets with 40 Gm (10 drams) of protein, if certain specific foods are taken each day, will provide sufficient calcium and iron, but the phosphorus content remains consistently low

3 Diets with 50 Gm ( $12\frac{1}{2}$  drams) of protein can be planned to provide an adequate mineral supply, but the margin of safety is small

4 Diets with 60 Gm (2 ounces) of protein can easily be planned to yield an adequate mineral supply

When the mineral requirement is too low over a prolonged period of time, nutritional anemia (from lack of iron), thyroid disease (from lack of iodine), bone disturbances (from lack of calcium and phosphorus) may be some of the resulting defects

**Protein Requirement.**—The minimum requirement of protein in the *optimum diet* is 40 Gm (10 drams) per day, according to Sherman, but 75 to 100 Gm ( $2\frac{1}{2}$  to  $3\frac{1}{3}$  ounces) daily will provide a liberal margin of safety for promoting growth, maintenance and repair of the body tissue

Milk, eggs, cheese and meats are sources of protein which have the highest biological value. In the *nephritic diet*, a reduction in the protein content is advised in order to decrease the strain on the kidneys. This can be as low as 20 to 25 Gm (5 to  $6\frac{1}{2}$  drams) per day for a short time in acute cases. Less than 40 Gm. (10 drams) sometimes results in nutritional edema, lessened effi-

ciency and stamina, and some authorities question early severity. Lately, the tendency has been to increase the protein allowance per day to 60 to 65 Gm (2 to  $2\frac{1}{3}$  ounces). This is especially beneficial in prolonged chronic cases, where normal nutrition must be maintained

The calculated diet bears out the preceding statements. (See next page.)

**TREATMENT OF EDEMA.**—A most interesting report is presented by F. H. Lashmet (J. A. M. A. 97:918 (Sept. 26) 1931), regarding the treatment of *nephritic edema* by acid. He considers that instead of the bodily fluids and chlorides being retained because of inefficient functioning of the kidneys, these substances may never be presented to the kidneys for excretion. He performed experiments to determine whether nephritic edema was influenced by (a) fluid intake, (b) chloride intake, (c) total ash intake or (d) reaction of the ash

He found that the edema varied independently of the increase or decrease in the fluid intake. The influence of chlorides on the question of edema was dependent upon the form in which they existed. Chlorides as sodium chloride increased edema, while in the form of **hydrochloric acid** it was decreased. Thus he found that the reaction more than the substance itself was important and the deciding factor. He also found that the reaction of the total ash intake is more important than the amount. Alkaline ash intake increases the edema, while acid ash decreases it. The author states that in the treatment of nephritic edema during the past 2 years, he has used a low protein, "salt poor" diet with a neutral ash to which are added acids or acid producing salts. The fluid intake has been pushed rather

DIET No 1—40 GRAMS

Food	Weight, Grams	Amount	Protein	Fat	Carbo- hydrates	Calories	Calcium	Phosphorus	Iron
Graham bread . . .	60	2 slices	5.4	1	30.6	154	0.03	0.13	0.0014
Farina . . .	100	½ cup	1.8	0.3	12.4	81	0.003	0.02	0.00014
Cornflakes . . .	20	⅔ cup	1.6	0.1	17.3	77	0.004	0.038	0.0005
Spinach . . . . .	100	⅓ cup	2.1	0.3	2.3	20	0.067	0.068	0.0066
Lettuce . . . . .	50	8 leaves	0.6	0.15	1.1	8	0.043	0.042	0.0001
Carrots . . . . .	100	⅝ cup	1.1	0.4	8.2	41	0.056	0.046	0.00107
Orange . . . . .	139	1	0.9	0.2	10.6	48	0.045	0.021	0.00066
Prunes . . . . .	100	3 prunes + 3 tbs. juice	0.6	..	30.9	126	0.054	0.105	0.00517
Baked potato . . .	100	1	2.2	0.1	18	82	0.014	0.058	0.00085
Canned pineapple .	100	½ cup diced	0.4	0.7	36.4	153	0.066	0.18	0.00258
Eggs . . . . .	100	2	13.4	10.4	..	148	0.086	0.067	0.0002
Cream . . . . .	100	½ cup.	2.1	41	1.5	383	0.24	0.186	0.00048
Milk . . . . .	200	1 glass.	6.6	8	10	138	0.0075	0.0085	0.0001
Butter . . . . .	50		0.5	47.5	..	384.5			
Sugar . . . . .	30			..	30	120			
Totals . . . . .			39.3	110.15	209.3	1963.5	0.7155	0.9695	0.01985

DIET No 2—50 GRAMS

Same as Diet No 1 plus milk, 300 c c, or 1 glass	9.9	12	15	207	0.36	0.279	0.00072
Totals . . . . .	49.2	122.15	224.3	2170.5	1.0755	1.2395	0.02057

DIET No 3—60 GRAMS

Same as Diet No 1 less 1 egg Add 100 grams of meat . . .	42.5 18.7	116.95 28.3	224.3	2096.5 329	1.0425 0.011	1.1495 0.202	0.01931 0.00160
Totals . . . . .	61.2	144.25	224.3	2425.5	1.0525	1.3515	0.02091

than restricted and the results for him have been quite favorable

**Diet in Edema.**—The recent work of F H Lashmet of the University Hospital of Michigan (J A M A 97 918 (Sept 26) 1931, Am Dietetic J (Dec 1 1931), presents a phase in the treatment of nephritic edema which is a departure from the previous method

The results of his work in the past 2 years indicate that edema is not necessarily influenced by fluid intake. He emphasizes the fact that the sodium ion in the sodium chloride is instrumental in increasing the degree of edema, rather than the chloride. Chloride has been tried in acid form such as hydrochloric acid or ammonium chloride and a decrease in edema is noticed, regardless of the fluid intake. Thus, when results indicate that the alkali ash is active in increasing edema, while the acid ash decreases it, it is evident that the result of the total ash intake is more important than the total amount of ash. In this case, all sources of alkali ash must be controlled. This necessarily changes the dietary procedures as the average diet is alkaline in reaction.

The recommendations in this treatment include a diet which will give a neutral reaction with an approximate content of 50 grams of protein. Fortunately, the diet may be served in general soft or liquid form, according to the condition of the patient. An acid producing salt, preferably ammonium chloride which may be given in doses of 10 to 15 Gm ( $2\frac{1}{2}$  to  $3\frac{3}{4}$  drams) daily, probably is administered best at meals in 0.5 Gm ( $7\frac{1}{2}$  grains) capsules. Ammonium chloride is more easily tolerated when given in this manner. It also liberates a large number of acid ions.

Lastly, the fluid intake may be increased to as much as 5000 c.c. (5

quarts) daily, without consideration of the edema, on the principle that the diseased kidney cannot concentrate urine. Therefore, the author claims it is illogical to restrict fluids, since the restriction would result in the patient being unable to eliminate all waste products. So far, no difficulty has been found in eliminating the forced fluids.

In discussing the still unsettled question of renal edema, J Harold Austin (J A M A 97 919 (Sept 26) 1931) points out that in chronic nephritis it is due to 4 factors, namely (1) The level of serum protein, especially the albumin fraction of the serum, (2) the acid or base preponderance in the ash of the intake, (3) the absolute intake of base; (4) the nature of the base in the intake, whether sodium or potassium, since the effect on edema of these 2 ions is different. In the management of edema all the factors must be considered, although the relative importance of each still remains to be decided.

The neutral diet outlined by Miss Gladys Enke, University Hospital of Michigan, follows the usual method of nephritic feeding by allowing approximately 2000 calories per day. The diet is salt free and 0.6 Gm (10 grains) of protein per kilo ( $2\frac{1}{5}$  pounds) of body weight is allowed and it emphasizes one definite factor—that practically all foods have an acid or basic reaction in the body. Hence, fruits and vegetables will be found basic, due to their content of calcium, magnesium, sodium and potassium, while meats and cereals, due to the sulphur, phosphorus and chlorine, are strongly acid. Thus, the foods producing an acid and basic reaction are planned to balance, but a slight acid excess is desirable. In the calculation of the diet, the following tables, which are self-explanatory, may be used

NEUTRAL DIET  
(By Miss Gladys Enke)

All foods listed in *Group A* are to be used, divided as desired

GROUP A

Food	Grams	Approximate Measure	Excess Acid
Cereal, prepared	20	$\frac{2}{3}$ cup	19
Or cereal, uncooked	20		.
Or cereal, cooked	100	$\frac{1}{2}$ cup	
Bread, whole wheat	90	3 slices	65
Rice, uncooked	30	2 tablespoonfuls	28
Or rice, cooked	100	$\frac{1}{2}$ cup	.
Macaroni, uncooked	30	$\frac{1}{4}$ cup.	28
Or macaroni, cooked	100	$\frac{2}{3}$ cup	.
Butter	60	4 tablespoonfuls	Neutral
Sugar	30	6 teaspoonfuls	Neutral
Tapioca, uncooked	10	1 tablespoonful	Neutral
Or tapioca, cooked	100	$\frac{1}{2}$ cup	Neutral.
Or cornstarch	6	1 tablespoonful	Neutral
Total excess acid			141

To this add one food from *Group B*

GROUP B

Food	Grams	Approximate Measure	Excess Acid	Total Excess Acid for the Day, A + B
Oysters . . . . .	200	8 large	30.4	44.5
Eggs . . . . .	100	2	11	25.1
Beefsteak, medium-fat	79	$3\frac{1}{2}$ in x $3\frac{1}{2}$ in x $\frac{1}{2}$ in	8.5	22.6
Lamb roast . . . . .	68	$3\frac{3}{4}$ in x $4\frac{1}{2}$ in. x $\frac{1}{4}$ in	7.3	21.4
Beef, round, lean . . . . .	68	3 in x $3\frac{1}{2}$ in. x $\frac{1}{2}$ in.	7.2	21.3
Lamb chop, E. P., medium-fat	72	$4\frac{1}{4}$ in x 2 in x $\frac{3}{4}$ in	6.7	20.8
Chicken, cooked . . . . .	48	$\frac{1}{2}$ leg or $\frac{1}{4}$ cup	6.7	20.8
Veal chop, E. P., loin, medium-fat	68	1 small, $\frac{3}{8}$ in thick	6.7	20.8
Pork chop, E. P., medium-fat	80	$4\frac{1}{2}$ in. x $2\frac{1}{4}$ in. x $\frac{3}{4}$ in	6.6	20.7
Fish . . . . .	58	3 in x $2\frac{1}{4}$ in x $\frac{3}{4}$ in	6.5	20.6
Veal roast . . . . .	50	2 in x $2\frac{3}{4}$ in x $\frac{1}{8}$ in	6.5	20.6

Thus *Group A*, plus one food from *Group B*, gives the total excess acid for the day

The amount of milk and cream in *Group C* is to be used either in combination with other food or as a beverage

Food	Grams	Approximate Measure	Excess Base
Cream, 20 per cent. . . . .	200	1 cup.	12
Milk . . . . .	200	1 cup	36
Total excess base . . . . .			48

The excess base of *Group C* must be subtracted from the total acid,  $A + B - C$ , the result being the amount of excess base which may be used in fruits and vegetables

Potatoes and leafy vegetables are so high in base that they may be used only occasionally. Cranberries, plums, prunes, and corn have an excess acid, hence they may be used to an advantage in the diet



## FRUITS

Food	Weight, Grams	Approximate Measure	Excess Base
Watermelon	100	2 $\frac{1}{2}$ in x 2 $\frac{1}{2}$ in x $\frac{1}{2}$ in	27
Grapes	100	$\frac{1}{2}$ cup or 24 grapes	27
Pear, fresh	100	1 medium	3.6
Apple, fresh	100	$\frac{1}{2}$ medium-size or 1 small	37
Grape juice	100	$\frac{1}{2}$ cup	39
Lemon juice	100	$\frac{1}{2}$ cup	41
Cherry juice	100	$\frac{1}{2}$ cup	44
Orange juice	100	$\frac{1}{2}$ cup	45
Raspberry juice	100	$\frac{1}{2}$ cup	49
Peach, fresh	100	1 medium	50
Lemon	100	1 lemon, 2 $\frac{3}{4}$ in long	55
Banana	100	$\frac{3}{4}$ cup or $\frac{1}{2}$ large	56
Orange	100	Pulp of orange, 2 $\frac{1}{2}$ in diameter	56
Cherries, fresh	100	$\frac{2}{3}$ cup	61
Apricots, fresh	100	2 apricots, 1 $\frac{5}{8}$ in diameter	68
Pineapple, fresh	100	$\frac{2}{3}$ cup, diced	68
Muskmelon	100	$\frac{1}{2}$ cup of pulp or $\frac{1}{3}$ of 4 $\frac{1}{2}$ in melon	75
Rhubarb	100	$\frac{1}{2}$ cup, cooked	86
Dates	100	14	11
Raisins	100	$\frac{1}{4}$ cup	237

## VEGETABLES

Food	Weight, Grams	Approximate Measure	Excess Base
Asparagus	100	$\frac{1}{2}$ cup, cut	08
Green peas, fresh	100	$\frac{3}{4}$ cup	13
Onions	100	$\frac{1}{2}$ cup or 3 medium-size	15
Pumpkin	100	$\frac{1}{2}$ cup, cooked	15
Squash	100	$\frac{1}{2}$ cup, mashed	28
Turnips	100	$\frac{1}{2}$ cup, cooked	27
Radishes	100	10 radishes, 1 in diameter	29
Mushrooms	100	$\frac{1}{2}$ cup, canned	4
Cauliflower	100	$\frac{2}{3}$ cup, cooked	53
String beans, fresh, raw	100	$\frac{2}{3}$ cup, cut	54
Tomatoes, fresh	100	$\frac{1}{2}$ cup, cooked, or 1 tomato 2 $\frac{1}{2}$ in diameter	56
Cabbage	100	$\frac{2}{3}$ cup, cooked, or 1 $\frac{1}{2}$ cup, raw	6
Tomato juice	100	$\frac{1}{2}$ cup	62
Sweet potato	100	$\frac{1}{2}$ , medium-size, uncooked	67
White potato, raw or steamed	100	1 potato, 2 $\frac{1}{2}$ in. diameter	7
Lettuce	100	16 small leaves or $\frac{1}{4}$ head plus 2 leaves	74
Celery	100	4 medium stalks or $\frac{3}{4}$ cup, cut	78
Cucumber	100	$\frac{1}{8}$ cup, sliced, or 3 in x 1 $\frac{3}{4}$ in diameter	79
Rutabagas	100	$\frac{1}{2}$ cup, mashed	85
Beets, fresh	100	$\frac{2}{3}$ cup	109
Carrots	100	$\frac{5}{8}$ cup, cooked	108
Parsnips	100	$\frac{1}{2}$ cup	119
Fresh lima beans	100	$\frac{1}{2}$ cup	14
Chard	100	$\frac{1}{3}$ cup, cooked	158
Spinach	100	$\frac{1}{3}$ cup, cooked.	27

FULL DIET  
(As Outlined by Gladys Enke)

*Sample Menu*

Food	Weight Grams	Approximate Measure
<i>Breakfast</i>		
Apricots, fresh	50	1 apricot, 1 $\frac{5}{8}$ in diameter
Oatmeal, uncooked	20	$\frac{1}{4}$ cup, dry, or 4 tablespoonfuls.
Soft-cooked egg	50	1 egg
Whole-wheat toast	30	1 average slice
Butter ..	10	1 teaspoonful
Milk . . . .	100	$\frac{3}{8}$ cup
Cream, 20 per cent	100	$\frac{1}{2}$ cup
Sugar .	10	2 teaspoonfuls
Coffee .		2 teaspoonfuls.
<i>Dinner</i>		
Creamed brown rice	30	2 tablespoonfuls, dry
Rice, uncooked . . .	5	$\frac{1}{2}$ teaspoonful
Butter . . . .	50	$\frac{1}{4}$ cup.
Cream, 20 per cent	100	12 stalks, 5 in.
Asparagus, fresh .	5	$\frac{1}{2}$ teaspoonful.
Butter		
Lettuce salad		
Leaf lettuce	40	Approximately 6 small leaves.
Mayonnaise	10	2 teaspoonfuls
Whole-wheat bread	30	1 average slice
Butter .	10	1 teaspoonful.
Sugar .	5	1 teaspoonful.
Pineapple tapioca		
Tapioca, uncooked	10	1 tablespoonful
Cream, 20 per cent	50	$\frac{1}{4}$ cup.
Pineapple, fresh	50	$\frac{1}{8}$ cup, diced.
Sugar . . . .	10	2 teaspoonfuls
Dates . . . .	10	1 date
Tea .		
<i>Supper</i>		
Baked macaroni		
Macaroni, dry .	30	$\frac{1}{4}$ cup.
Milk . . . .	100	$\frac{3}{8}$ cup
Grilled tomato .	100	1 tomato, 2 $\frac{1}{2}$ in diameter
Egg salad		
Egg . . . .	50	1 egg
Lettuce . . . .	20	Approximately 3 small leaves.
Radish roses .	25	2 or 3
Mayonnaise	10	2 teaspoonfuls
Fresh pear	50	$\frac{1}{2}$ medium
Whole-wheat bread .	30	1 average slice
Butter ..	10	1 teaspoonful
Sugar ..	5	1 teaspoonful
Tea . . . .		

Liquid Diet  
As Outlined by Gladys Erbe

Food	Weight Grams	Proteins	Fat	Carb- hydrates	Calories	Excess Acid	Excess Base
Cream, 20 per cent	300	87	60	12	624		18
Cream, 40 per cent	100	22	40	3	381		04
Milk	400	132	16	20	276		72
Eggs	3	201	156		222	165	.
Fruit juice, grape	100	03		173	70		4
Vegetable purée, tomato	50	05	01	11	11		28
Sugar	30			30	120		.
Butter	40	04	34		308		.
Cereal (oatmeal, un- cooked)	10	16	07	66	39	12	
Totals		47	1664	90	2051	177	162

The diet may be prepared in a liquid or soft form. Fruits and vegetables may be puréed, and the caloric requirement may be regulated by increasing or decreasing the amounts of butter and sugar, or substitution of 40 per cent whipping cream in place of 20 per cent. coffee cream.

**NEPHRITIS IN CHILDREN.—**  
**CLASSIFICATION**—It has always been difficult to classify the different types of nephritis of children into distinct groups. A following classification of nephritis as it occurred in a large series of children, with the relative frequency of the different forms, has been reported by C. A. Aldrich (Am J. Dis. Child 40: 678 (Sept.) 1930):

	Patients
1 Acute postinfectious hemorrhagic nephritis	129
2 Chronic nonspecific nephritis	24
3 Nephrosis	20
4 Subacute bacterial endocarditis with nephritis	5
5 Syphilis with nephritis	3
6 Renal infantilism	3
7 Tuberculosis with nephritis	2

The prognosis of the patients making up the first group is by far the best. In this series, 62 per cent of that group died; of the second group 54.2 per cent died; while in the third group 35 per cent died, and 25 per cent additional still had symptoms of the disease. None of the last 4 groups survived.

A very similar though more simple classification of the kidney diseases of

childhood has been offered by A. G. Mitchell (Am J. Dis. Child 40: 101 (July) 1930). From a clinical standpoint, he divided them into:

1 Acute hemorrhagic (glomerular) nephritis

2 Acute edematous (tubular) nephritis (sometimes called nephrosis).

3 Chronic nephritis which is usually diffuse but in which glomeruli, tubules, blood-vessels or interstitial tissue may be involved to a greater extent than in the remainder of the kidney structure.

4. Suppurative nephritis which may be acute or chronic.

5 Lipoid nephrosis.

An analysis of 99 cases of *acute nephritis in children* by J. D. Lyttle and L. Rosenberg (Am J. Dis. Child 38: 1052 (Nov.) 1929) showed 74 to be acute glomerular, with 17 acute diffuse and 8 acute tubular. In the great majority of cases the authors point out a respiratory infection preceded the nephritis. Scarlet fever was found to be rare as a causative agent. The mortality rate was 11 per cent. Fifteen per

cent of the cases became chronic as a result of a chronic or persistent infection or repeated acute infections of the respiratory tract, middle ear or sinuses. The degree of edema, hematuria, hypertension and nitrogenous retention had little relation to the chronicity of the disease.

**PATHOLOGY.—Nephrosis.**—In an investigation of the clinical and pathologic manifestations of 8 patients with so-called nephrosis, S B Wolbach and K D Blackfan (Am J M. Sc 180:453 (Oct) 1930) conclude that this disease could not be said to have its origin in the kidney, nor did the other different manifestations of it seem to be referable to the kidney damage alone. The tubules of the kidney were the structures most severely damaged, while the glomerular lesions apparently occurred only in the later stages. The damage found in the liver and thyroid tissues was thought to have been due chiefly to an overtaxing of their capacity and secondary to increased functional demands.

The *edema* which almost always occurs in nephrosis has been the subject of additional study during the past year. It is usually accompanied with a low protein and a high cholesterol content of the blood. The relationship of these phenomena to one another has been investigated by J K Clavin and A. H. Goldberg (Am. J Dis Child 41:1066 (May) 1931). Twelve patients with evidence of nephrosis and considerable edema had large amounts of cholesterol in their blood. When the edema became less marked or disappeared entirely, the cholesterol diminished in amount but did not return to normal amounts. In a few instances the cholesterol rose during periods of loss of edema. The relationship between the

degree of cholesteremia and edema did not appear to be close enough to suggest that one was dependent on the other. The increase of the amount of cholesterol in the diet of these patients did not affect in any way the amount of blood cholesterol. It was thought likely that the cholesterol arose from a disturbance of fat metabolism which accompanied the nephrosis.

A much more definite relationship was demonstrated in the serum protein content and the *edema*, by the same investigators (*Ibid* 42:314 (Aug) 1931). In the same 12 patients the edema was accompanied by a lowering of the serum albumin to 2 to 2.5 per cent, with the exception of 2, who had no edema and yet had only 0.75 and 0.29 per cent serum albumin. The globulin portion of the blood remained much more constant and occasionally increased in amount so that the albumin-globulin ratios were disturbed. As a rule, the serum albumin decreased as the cholesterol content increased, but here again, the variations in this ratio were so numerous that no definite relationship between the two could be established and it is unlikely that the cholesterol increase is merely a "compensatory mechanism." Calvin and Goldberg were unable to cause a rise in the blood proteins of their patients by giving them diets high in protein, nor did the high protein diet have any appreciable effect on the edema. The edema of the patient varied more rapidly than the change in the level of the albumin of their blood, which led to the conclusion that the low protein levels were in themselves not the cause of the edema.

Different results in regard to the influence of a high protein diet on the reduction of the *edema* of a patient with nephrosis were reported by D. M.

Cowie, K. M. Jarvis and M. Cooperstock (*Am. J. Dis. Child.* 40:465 (Sept.) 1930) They observed that a diet high in protein caused an increase in the output of protein in the urine at first, but within a short time the amount eliminated returned to the previous level. The nitrogen content in the stools did not vary appreciably during the change to a higher protein intake. Since the output of nitrogen did not materially increase with the added intake, it was thought that the protein was stored in the body tissues. A positive nitrogen balance of 1 to 375 grams was apparently instrumental in keeping the body free from edema in this series of patients. Although the edema disappeared and there was a clinical improvement in the patients, the albumin content of the urine remained high and usually there was a reversed albumin-globulin ratio in the blood serum. However, as long as the blood contained more than 5 grams of protein, the patients were free from edema.

**Nephrosclerosis.**—In a review of the subject of nephrosclerosis, A. G. Mitchell (*Am. J. Dis. Child.* 40:101 (July) and 345 (Aug.) 1930) stated that the cause of the bone changes which accompany chronic kidney disease of this type may be due to the inability of the elimination of phosphates through the urine. This results in the excretion of large amounts of phosphate by way of the intestinal tract and here they combine with calcium to form insoluble calcium phosphate which cannot be absorbed. The deficiency of calcium leads to the disturbance of bone formation and signs similar to rickets. In a study of the case histories of all the patients previously reported with this disease and of 6 added patients observed by himself, the author has discovered many

instances in which there was a family predisposition to the disease. In very few of the patients was syphilis the etiologic factor. Rarely was the disease manifest in early childhood but became more evident later when increased demands of rapid growth or infection, especially of a streptococcal type, produced a strain on metabolic processes. The early symptoms of the disease were usually the retardation of growth, together with a polyuria and a polydipsia. Other frequent signs and symptoms were headache, vomiting, occasionally convulsions of uremic nature, cardiac enlargement, elevated blood-pressure, anemia, a low specific gravity of the urine with an increased albumin content and a marked renal insufficiency. An albuminuric retinitis was frequently observed, while less common symptoms were edema, signs of tetany, and sclerosis of superficial blood-vessels. Congenital cystic kidneys often gave symptoms and signs similar to those of nephrosclerosis and it was of interest to note that the tubules in the former disease were the portions of the kidney which were primarily affected.

**PROGNOSIS.**—The prognosis of *nephrosclerosis* is usually very poor, the average age at the time of death of 129 patients with the disease observed by Mitchell (*loc. cit.*) being about 9½ years.

Thirty-four children who had had *acute glomerular nephritis* were observed 1 to 12 years later by H. G. Guild (*Bull. Johns Hopkins Hosp.* 48:193 (Apr.) 1931). The ages of the children at the time of the acute nephritis ranged from 2 months to 13 years. With the exception of one girl who had rheumatic heart disease, all the patients were symptomless. However, 5 had a persistent albuminuria which was not

due to any other apparent cause except that of the previous acute nephritis. None had impaired kidney function. In regard to the remainder, the urine in the majority of instances had become clear within 2 months after the original infection. The improvement had occurred more quickly and in a higher proportion in the younger children and, therefore, the prognosis of the disease was thought to be better in younger patients. The albuminuria persisted in some instances for a year or more without impairment to health, and then the urine became clear. Those who still had foci of infection remaining were not in as good condition as the others.

The prognosis of *acute glomerulonephritis* in children has also been reported by R. Levy (Jahrb f Kinderh. 130:215 (Jan) 1931). Of 120 children with this disease, 9 had died, 7 during the acute stage and 2 some time later while still suffering from chronic forms. At a later period, 54 of those who survived were reexamined and 26 were thought to be normal; 1 had a definite chronic form of nephritis, while 4 had changes of some type which could not be diagnosed definitely, but probably were remnants of the disease.

**TREATMENT.—Acute Glomerulonephritis.**—Treatment of acute glomerular nephritis in children with x-ray radiation has been tried by G. Salvoli (Pediatria 38 361 (Apr. 1) 1930) with favorable results. The rays were directed over an area extending from the tenth dorsal to the second lumbar vertebra. Among 12 children receiving this treatment during the acute stage, all but 4 had some relief which was manifested either by an increased urinary output or a diminution of the amount of blood in the urine. The author believed the rays acted primarily

on the nerves supplying the kidney, especially in causing a relaxation of the blood-vessels when conditions of hypertonicity existed.

**Nephrosis.**—Calcium gluconate has been used with success in the treatment of *edema* of 3 nephrosis patients by W. S. O'Donnell and S. J. Levin (J A M A 96 837 (Mar 14) 1931). The drug was administered subcutaneously and intramuscularly in doses of 10 cc (2½ drams) to 2 children, aged 4 years and 1½ years respectively, while to the third child of 10 years 155 cc (5½ ounces) were given. There was considerable loss of edema and even some evidence of dehydration. The appetite and general health of the children improved. A diet sufficient in protein was given at the same time.

**Thyroid extract** in large doses seemed to be very helpful in the treatment of 3 children with nephrosis, according to S. J. McClendon (J A M A 94.1202 (Apr 19) 1930). These patients, aged 8, 9 and 12 years respectively, had low basal metabolic rates in conjunction with the other symptoms of nephrosis. Dietary regulation, the treatment of foci of infection, and drugs were employed also but the administration of thyroid gland extract was apparently the most effective measure. Large doses of 9 to 10 grains (0.58 to 0.65 Gm) were given daily for about a week and then 3 to 6 grains (0.2 to 0.4 Gm) were administered daily until there was clinical improvement. A greatly increased output of urine, together with a reduction in the edema, resulted.

Patients with nephrosis have considerable tolerance to *thyroxin*. Ten times the amount of thyroxin may be given to such patients as to persons with myxedema, according to R. Platt (Quart. J. Med. 23:129 (Oct.) 1929).



This high tolerance of nephrosis patients could not be explained by low basal metabolic rates because only 60 per cent of nephrosis patients have low metabolism. The two other possibilities of explanation of the high tolerance were (1) a destruction of thyroxin or inhibition of action, or (2) a rapid excretion. In order to determine whether this latter theory was tenable, the amount of thyroid excreted in the urine by nephrosis patients was estimated by a series of tests on tadpoles. Only a small amount of the drug was found to be eliminated in this manner so that the author was forced to conclude that nephrosis patients owed their high tolerance to this drug, either to a rapid destruction or an inhibition of its action.

**NEPHROLITHIASIS.—ETIOLOGY.**—Regarding the condition of nephrolithiasis, V. Blum (Wien klin Wchschr 44:602 (May 8) 1931) summarizes as follows: The observation of the medical practitioners as well as the statistics of the surgeons and urologic clinics of central European States prove that since 1924 there has been a steady increase in the frequency of nephrolithiasis. A study of the geographic distribution of nephrolithiasis indicates a certain antagonism between lithiasis and goiter. In experiments on animals it could be proven that a diet deficient in vitamins regularly produces urinary calculi. In metabolic experiments it was found that hormonal influences are also significant in calculus formation and that salt retention and elimination are influenced by the thyroid hormone. The influence of the vitamin deficiency or of the disturbance of the hormonal equilibrium becomes manifest as a disturbance in the colloidal content of the urine which, in turn, facilitates a pre-

cipitation of the calculus-forming salts and crystals. The wave of nephrolithiasis is an outcome of an epidemic developing hormonal and metabolic disturbances. Mistakes which may lead to endocrine and to metabolic disorders are still being made. This is proven by the misuse of iodine preparations in thyrotoxicosis. Not only because of the danger of thyrotoxicosis, but also because of the formation of renal calculi, the misuse of iodine medication and the reducing preparations containing iodine should be warned against. The rules in regard to diet of persons predisposed to nephrolithiasis have to be revised, according to Blum. One-sidedness in nutrition is to be avoided. A pure meat diet, as well as vegetarianism and a raw diet, are wrong and not only a vitamin deficiency but also hypervitaminization has to be guarded against.

The most common origin for the formation of calculi consisting of phosphates and carbonates with an organic nucleus are the chronic forms of staphylococcuria described by L. Hellstrom (Acta chir Scandinav 55:545, 1929). This stone formation is believed to be due to the ability of the staphylococci to decompose urea, thereby creating a reaction favorable for the precipitation of the alkaline salts. The treatment of such staphylococcuria and the calculi attendant is not only for the stones themselves but also the staphylococcuria.

C. P. Mathe (J. A. M. A. 95:657 (Feb 28) 1931) gives a most interesting discussion of the present day management of renal stones. He states that this subject has received more attention than any other lesion of the kidney but, in spite of all this interest, certain methods still are practiced and benign operations are continued which seem to favor the recurrence of stones.

According to the author, the etiology of stones is still an undecided question but in many individuals he believes it is due to a chemical and metabolic change dependent on the food intake. He cites the work of Holmes and Caplan, who attribute the high incidence of renal stones in Florida to the excessive intake of fruits and vegetables, the alkaline ash-producing foods overwhelming the protective mechanism in the urine, resulting in the formation of stones.

In many instances, Mathe believes that the stones are the result of a renal stasis as he has found many stones in the bladder where there is an existing hypertrophic prostate or a urethral stricture. Congenital abnormalities of the kidney through their stasis also favor the development of calculi. Infection also plays a rôle. The bacteria cohere by aid of a mucinous cement material present, on top of which urinary salts are readily precipitated.

The presence of an infection often predisposes to a secondary development of stones. This is exemplified by the occurrence of a prompt disappearance of inflammatory processes following the removal of calculi.

In the end-result, the author states that it makes very little difference whether the infection is directly the cause of the stone formation or whether the stone is the cause of the infection. The hesitancy to remove the stone often results in infection of the kidney and pressure and irritation cause necrosis and abscess formation. First there develops a local infection, frequently a solitary abscess, then a suppurative nephritis, followed by way of the lymphatics or by direct extension by an infection of the perinephric tissue and even in some instances to a collection of

purulent material above the level of the diaphragm.

**PATHOLOGY.**—E. Sacharoff (*Ztschr f Urol* 24 827, 1930) reports the case of a man, aged 33 years, who had never had attacks of severe abdominal pain or disturbance in urination, but in whom x-rays disclosed a large number of stones in the left kidney. This kidney was removed and on sectioning it was found that the pelvis was greatly dilated and the kidney consisted of several cavities that contained large numbers of stones of various sizes. A large proportion of the renal parenchyma was destroyed and when the stones were counted they numbered 3000 and their weight collectively was 21.5 grams ( $5\frac{1}{4}$  drams). All the stones were calcium phosphate. The absence of colic was explained by the fact that one of the larger stones had blocked the junction of the pelvis and the upper end of the ureter and prevented any small ones from passing down the ureter.

**DIAGNOSIS.**—An interesting paper written by A. L. Chute (*Minnesota Med* 12 731 (Dec) 1929) gives a discussion of the recognition and treatment of renal lithiasis. The author believes the stones which are held firmly in the kidney, especially those which are large and cause atrophy of the parenchyma, predispose to suppuration, do not cause marked symptoms as do those smaller ones which block the renal outlet, and cause an acute renal pelvic distention. In x-rays of the urinary tract it is most important, as stressed by the author, to have the patient's digestive system thoroughly liberated of all material. The most common conditions which may produce shadows which may be confused with stones are gas, gallstones, calcified abdominal glands, phleboliths and calcified vessels.

**PROPHYLAXIS** — An interesting relationship has been found between the food content and the density and composition of stones of the upper urinary tract by O Grant and V Simpson (Southern M J 23 628 (July) 1930). They classified 29 renal and ureteral calculi according to their density and chemical composition. Calcium was present in 85 per cent, ammonium in 62 per cent, magnesium and phosphate in 51 per cent, oxalate in 24 per cent, urates chiefly in 20 per cent, carbonate in 13 per cent, and cystine in 6 per cent. The authors stress the importance of food and diet in the prevention of the recurrence of stones. Surgery may remove the initial stone or stones, but the conditions necessary for the subsequent production may again obtain. A suitable diet may keep the uric acid content of the urine below the supersaturation point, thus preventing the completion of the circle of factors considered essential for the formation of stones. A purine-free diet is not practicable, but a low purine diet is. A proper diet is of equal importance in the prevention of the formation of subsequent stones.

**TREATMENT.**—J. Salleras (Semana méd 2 1221 (Oct 31) 1929) observed 135 cases of renal or ureteral stones and states that he treated them medically only (1) when there was an abundant elimination of gravel and absence of stones; (2) when the stones were small and hence could easily be expelled through the ureter; (3) in the presence of bilateral insufficiency of the kidneys, and (4) when the patient refused surgery. The author considered **surgery** the best treatment for either form of stone and stated that the type of operation is determined according to the size, form, position and number of stones, as shown in the x-rays. Of the

entire group studied, operated or not, by the author, 61 were cured, 42 were improved, 24 remained in the same condition, and 8 died. The principal cause of mortality continues to be a secretory anuria, especially when nephrolithotomy is done.

Chute (*loc cit*) believes that the presence of 1 stone in 1 kidney is a more important indication for immediate surgical intervention than when the stones are bilateral. He believes the kidney which shows the better function should be operated first. In Chute's opinion, it is a mistake to drain a renal pelvis through a pyelotomy wound, especially by tube drainage, as stubborn fistulae have followed this procedure. After removal of the stone, he believes the surgeon should be able to pass a probe through the ureter and into the bladder without perceiving a sensation of grating.

In treating kidney stones, Mathe emphasizes the importance of conservative procedures for the renal tissue and the prevention of recurrence of the stone. To him this consists in the employment of the proper operative procedure when it is decided upon by the size, shape and position of the stone. Stones measuring less than 5 mm may usually be induced to pass by means of **cystoscopic manipulations**. When the stone has a diameter above 6 mm, the author believes the surgeon should resort to an **operative procedure**. The several types of operation, their indication, technic and results are described.

An x-ray should be taken before the patient is released from the hospital, to rule out the possibility of the presence of small fragments of the stone. The author also advises routinely skiagrams made every 3 to 6 months and the urine carefully analyzed for pus and

blood If the latter is found either micro- or macroscopically, it usually is the signal for the recurrence of stones

**NEPHROSIS.**—T Izod Bennett (Lancet 1 115 (Jan 17) 1931) discusses the work of Epstein, in which he claimed to bring about a cure of the edema of nephritis by the employment of diets abundant in protein together with the administration of thyroid extract. About the same time, a group of German workers reported their observations upon a series of patients in whom the renal lesions were in the tubules and of a degenerative nature and were called "nephroses," as suggested by Muller. As time went on the term "nephrosis" has been accepted by Epstein and his co-workers to include such cases as lipoid nephrosis, chronic nephrosis or essential nephrosis. Much confusion has arisen, according to the author, as a result of calling many cases of nephritis with edema in addition to raised blood-pressure and nitrogen retention "*nephritis of the nephrotic type*" Many pathologists have taken exception to any classification which implies that degeneration is anything other than the first stage of ordinary inflammation.

The author gives a very interesting table—which follows—of the clinical, biochemical and pathologic features

which must be present and certain others which must be absent to classify any individual case as nephrosis

Thus from the table it will be seen that the case must (1) exhibit edema and albuminuria and (2) that there must be no evidence whatsoever of involvement of the cardiovascular system

About a year ago Christian called attention to the scarcity of cases from the postmortem examinations to support the theory of the existence of such a disease entity and he doubted its existence. Many Americans replied that they believed the condition to be benign and many cases recovered and, therefore, did not provide autopsy material. To this reply Bennett could not agree. The author reports a case which he terms typical of nephrosis and refrains from the use of the words "*lipoid nephrosis*" because cholesterol is almost always present in excess in the blood of many cases of nephritis in addition to edema and cardiovascular changes, making them not alone features of nephrosis.

*Etiologically* many cases of intense albuminuria and edema have been traceable to the prevalence of syphilis and with the advent of specific treatment of the infection they have recovered complete health. Other cases of nephrosis appear to be tuberculous in origin and amyloid disease appears to

CHARACTERISTICS OF NEPHROSIS

	Positive	Negative
Clinical	Albuminuria Edema (lipoids in urine)	Normal blood-pressure and heart Normal retinae No hematuria No epithelial casts
Biochemical.	Increased blood cholesterol Diminished plasma proteins Reduced basal metabolic rate	Blood urea, chlorides, etc., normal
Pathological	Degeneration of renal tubules (lipoid infiltration)	Normal glomeruli and vessels

be essentially the same in many of its features. When this has been said there is very little to mention concerning the etiology, but the author points out the negative fact that a history of severe scarlet fever or of recurrent tonsillitis always makes it probable that the case belongs to the category of glomerulotubal nephritis rather than nephrosis.

The *prognosis* of such cases is certainly guarded, according to the author, and unless some definite etiologic factor like syphilis may be determined and treated, the opinion must remain doubtful for a long time regarding the subject of a permanent cure.

The author stresses the importance of the subject of nephrosis in regard to its relation to the production of *edema*. He points out that the symptoms of nephrosis are relatively simple, being merely albuminuria and edema and no changes in the blood chemistry save an excess of cholesterol and reduction of the plasma proteins. Probably the edema is the result of the loss of proteins from the blood plasma which follows the intense and prolonged albuminuria.

**COMPLICATIONS.—Edema.**—To Bennett (*loc. cit.*), generalized edema, as seen in the wards of the general hospital, is the result of the passage of water and salts through the capillary walls into the tissue spaces. There may be an increased permeability of the vessel walls, but some force must be present to bring about the passage of fluids into the tissue spaces. Two of these forces are outstanding in their importance. They are (1) the capillary blood-pressure and (2) the colloid osmotic pressure of the plasma proteins. The first of these forces is controlled in some measure by the general systemic blood-pressure. Turning to the second

great force, it has been recognized since the pioneer work of Starling that the molecules of protein in the plasma exercise a continuous osmotic pressure, tending to retain water and salts in the circulating blood. Fibrinogen has little power in this respect, globulin has more, but it is essentially the albumin which exercises the greatest osmotic force. Govaerts has calculated that the albumin molecules exercise a colloid osmotic pressure 6 times as great as that of globulin. It is this colloid osmotic pressure which is responsible for holding back water during the passage of the blood through the capillaries and for reabsorbing water from the tissue spaces when transudation has occurred. From this point it naturally follows that if for any reasons the plasma proteins are greatly decreased, the reabsorption of water will be impeded and the production of edema notably facilitated. In many instances the loss of albumin through the kidneys is so great that the plasma proteins diminish from their normal figure of about 8 grams per 100 c c to 6, 5 or even 4 or less.

**Treatment of Edema.**—Bennett (*loc. cit.*) concludes that from the observation on the subject of plasma-proteins, the very unsatisfactory method which was formerly adopted for treating these cases of edema is apparent. It is clear that to promote diuresis is not by itself an action tending to cure, because the mere extraction of water and fluids from the tissues does not stop the depletion of the plasma-proteins or prevent their leakage in the form of albumin in the urine. The only satisfactory cure will be one which will stop this leakage and return the plasma-proteins to their normal quantity. Diet is, therefore, a very important factor and even if present knowledge is insuf-

ficient to promote the creation of serum-albumin with any certainty, it is at least logical to keep these patients on a diet containing abundant protein which will supply them with the elements necessary to combat the constant loss of albumin which is the essential mechanism of their edema

### NEURONITIS, INFECTIVE.—

H G Jacoby (Arch Int. Med 48:764 (Nov) 1931) reports an additional case of infective neuronitis, giving credit to J R Bradford for recording the first 30 cases, and to F. Kennedy for the succeeding 4 cases

**ETIOLOGY.**—Material from fatal cases of infective neuronitis, when cultured on serum agar, yields minute, semitranslucent colonies, after 1 week, which then grow rapidly and assume a faint yellow color. When the culture is 12 or 14 days old, there is a continuous yellow-brown layer on the surface of the agar, while beneath the surface the agar becomes opaque. The organism has not been subcultured beyond the fifth generation. The nerve tissue to be cultured is placed in glycerin and kept there until contaminating organisms are found to be absent by culture, both aerobic and anerobic; it is then placed in the culture tube in juxtaposition to a piece of kidney from a thoroughly bled guinea-pig, and covered with nutrient serum agar made with attenuated serum of rabbit or horse, and slanted. The culture is rendered anerobic by covering with an inch of liquid vaseline.

Young cultures of the organism thus grown, by film preparation and suitable staining, show under the microscope a minute, rounded, oval or kidney-shaped organism, measuring 0.2 to 0.5 microns. Older cultures give indefinite staining bodies, with indefinite outline.

The virus has been passed successfully through monkeys, which clinically and pathologically demonstrated the same disease.

**PATHOLOGY.**—Autopsy revealed no changes in the dura and pia mater. The cerebral cortex was markedly congested, with small round cells. The pons and subthalamic regions were likewise infiltrated. The Purkinje cells were reduced in number and markedly degenerated in the cerebrum. In the spinal cord there was a diffuse degeneration of neurones, accompanied by a low grade chronic inflammation, throughout the anterior horn cells, the nerve fibers, the spinal ganglion cells and the sensory tracts of Goll and Burdach.

### SYMPTOMS AND DIAGNOSIS

—This disease is characterized by a febrile period of acute onset, with sore throat, headache, vomiting and pains in the back and limbs; this period lasts 1 or 2 days, and is followed by one lasting from 3 days to 6 weeks, in which the patient is symptom-free and apparently well. The third stage of the disease is inaugurated by the sudden development of paralysis of the large muscles of the thighs. At the beginning of this stage of the disease neurological signs are negative, but soon there is noted a gradually increasing ascending flaccid paralysis and a facial paralysis, usually bilateral, and of the infranuclear type, with complete loss of all the tendon reflexes, the ankle jerk and plantar reflex. General peripheral neuritis ensues late in the disease, with diplopia and difficult swallowing. Jacoby's case showed some loss of rectal and bladder control prior to the onset of a terminal bronchopneumonia, approximately 3 months after acute febrile onset, and 6 weeks after the onset of muscle weakness in the thighs.



**NEWBORN, DISEASES OF THE.—HEMORRHAGE.**

—In a statistical review of the symptoms and pathologic findings of 103 infants with evidences of *intracranial hemorrhage* at birth, G B Fleming and E D Morton (Arch Dis Childhood 5 361 (Oct) 1930) concluded that a xanthochromic cerebrospinal fluid was usually an indication of this lesion. When hemorrhage occurred in prematurely-born infants, the mortality was very high (75 per cent). In the group as a whole, the mortality was 48 per cent. The subsequent course of infants who survived a year or more was followed in 33 instances, and only 5 had persistent mental or physical defects. In postmortem examinations the most frequent lesion found was a tear of the tentorium. Although the *etiology* of the hemorrhages was difficult to determine, about half the number were apparently the result of a difficult labor, while the duration of labor seemed to have little or no bearing on the etiology; in fact, the mortality from hemorrhage in those infants who were delivered in normal time was slightly higher than that of infants born by prolonged or precipitate labor. In regard to the *signs and symptoms* of intracranial hemorrhage, convulsions occurred in about half the number of patients and cyanosis was a fairly common finding. Retinal hemorrhages were observed in 47 per cent of 81 patients whose fundi were examined, while in a group of 349 healthy infants, retinal hemorrhages were found in 25 per cent.

D Munro (New England J Med 203 502 (Sept. 11) 1930) also reviewed the *symptoms* of 117 infants with *cranial or intracranial injury*. Lesions of this type were most frequent in first-born infants and the most com-

mon symptoms were hyperreflexia, a weak cry, cyanosis, a failure to nurse properly and irregularities of respiration. The pressure of the cerebrospinal fluid was almost always increased in this series. Treatment consisted of withdrawing the cerebrospinal fluid by lumbar puncture, keeping up the nutrition, and maintaining fluid intake by mouth or by some parenteral route, and finally, the administration of oxygen for the relief of cyanosis.

In the necropsies of 50 infants who died of *intracranial hemorrhage*, H Yagi (Jap J. Obst and Gynec 12 335 (Dec) 1929) found the location of the lesion to be subdural in 88 per cent, leptomeningeal in 26 per cent, intraventricular in 18 per cent, intracerebral in 10 per cent, and epidural in 6 per cent. It was thought that many infants with asphyxia owe that symptom to intracranial hemorrhage.

W H Chase (Surg Gynec Obst 51 31 (July) 1930) analyzed the findings of 32 newly-born infants who died with *subdural hemorrhage*. The most common predisposing cause of hemorrhage in infants born with spontaneous delivery was prematurity. In prolonged labor it was thought that the molding of the head in the birth canal was as responsible for intracranial hemorrhage as the manipulations of the obstetrician. The site of hemorrhage in this series of infants was primarily subdural, usually above the tentorium and apparently due to a rupture of tributaries of the great cerebral vein near its junction with the straight sinus. Splitting of the tentorium and intradural hemorrhage did not appear to be serious lesions in themselves. In regard to the *symptoms* of intracranial hemorrhage, 90 per cent. of this group of 32 patients had only a slight cyanosis together with

shallow or labored respiration. Other signs which were present in a few instances were bulging of the anterior fontanelle, convulsions or spasmodic twitchings of the face or extremities.

A further study of the cerebrospinal fluid of premature infants has been made by J. Glaser (*Am J Dis Child* 40:741 (Oct) 1930). In 94 patients examined at necropsy 35, or 37 per cent, had evidence of *meningeal hemorrhage* or "meningeal congestion." Of these 35 patients, 28 had gross blood in the fluid. When routine punctures were done on all premature infants, an improvement was noted in those with symptoms of intracranial hemorrhage and the mortality from this condition decreased. It was thought that the reduction in the intracranial pressure and the drainage of the blood was responsible for the relief of symptoms. Xanthochromia of the spinal fluid (proved not to be blood by the benzidine test) was an almost universal occurrence in premature infants. The degree of the xanthochromia ran parallel to the amount of bilirubin in the blood serum of the patients. When the spinal fluid gave a positive benzidine test, it was an indication of hemolyzed red blood corpuscles and always indicated hemorrhage. A direct van den Bergh reaction of the spinal fluid also suggested hemorrhage. Fifty per cent. of the infants suffering from meningeal hemorrhage had spinal fluids which gave negative benzidine tests, which was explained by the supposition that the hemorrhage was recent and there had not yet been any hemolysis of the red blood corpuscles. The paroxysmal and intermittent cyanotic attacks in infants with intracranial hemorrhage were thought to be due possibly to intermittent pressure of a blood clot on the medulla oblongata.

*Hemorrhage into the abdomen, chest and elsewhere* has been observed in newly-born infants by B. Lundquist (*Acta obst et gynec Scandinav* 9:331, 1930). In 52 infants there were 3 who had hemorrhages in the chest, 2 of which were in the thymus gland, 1 in the mediastinum. Of 49 instances of abdominal hemorrhage, 5 were in the parenchyma of the liver, 14 from beneath the liver capsule, 18 in the suprarenal glands, 12 intraperitoneal and 1 as a result of rupture of the spleen. No definite etiologic factor was discovered, but it was thought that certain hemorrhagic diseases, syphilis, trauma or alterations of circulation at birth might be contributory causes.

S. Genell (*Acta obst et gynec Scandinav* 9:180, 1930) reported 3 instances of *rupture of the liver* which he had observed in newly-born infants, and 4 previously cited in the literature. Two occurred in children of the same mother and the author suggested as the cause either certain mechanical difficulties of labor or the possibility of a blood dyscrasia of some sort.

*Massive hemorrhage in the suprarenals* was noted in 4 newly-born infants by D. P. Arnold (*Am J Dis Child* 40:1053 (Nov) 1930). The onset was on the third to seventh day after birth with symptoms resembling shock, listlessness, refusal of food, rapid breathing, progressive anemia and occasionally convulsions. The abdomen was distended and rather boggy but there was no discoloration or mass. **Blood transfusion** was the treatment recommended.

#### ICTERUS NEONATORUM.—

**Etiology.**—The theory that icterus neonatorum is produced by a rapid destruction of red blood corpuscles liberating hemoglobin into the serum is sub-

stantiated by the results of certain experiments by A. Goldbloom and R. Gottlieb (New York State J. Med. 30:1219 (Oct. 15) 1930). They observed that the red blood corpuscles of newly-born infants were less resistant to dilutions of saline solutions. Normal red corpuscles usually begin to hemolyze in dilutions of saline of about 0.4 or 0.3 per cent. Some of the cells of the newborn hemolyze even in physiologic salt solution and many more in dilutions of 0.8 to 0.4 per cent, while certain others were as resistant to the dilutions as were normal red corpuscles. The more fragile cells consisted of immature nucleated and reticular types. In the blood taken from the umbilical vein of these infants, a low oxygen saturation was also discovered which resembled the condition of the blood of persons living in high altitudes. The next step of the investigators was to produce this condition experimentally. A group of guinea-pigs was kept in half an atmosphere of pressure with the result that a 30 per cent increase in the number of red blood corpuscles occurred. Many of these new cells were reticulocytes. After 10 to 15 days, the animals were returned to normal conditions and there was a rapid fall in hemoglobin and the red count, with a simultaneous rise in the icteric index of the blood and the development of an indirect van den Bergh reaction in the serum. The human fetus which is probably supplied with an insufficient amount of oxygen by the placental circulation and which has a mixture of arterial and venous blood in its circulation, is forced to develop a polycythemia. At birth, the fetus no longer needs the extra number of red blood cells and the destruction of the excess is probably the explanation of the jaundice.

*Pathology.*—I. Aschoff and R. Hummel (Virchow's Arch. f. path. Anat. 275:1 (1930)) have observed that bilirubin in infants with icterus neonatorum occurs in a crystalline form, a phenomenon mentioned many years previously by Orth. In other types of jaundice, especially the adult forms, bilirubin is not found in this state except very rarely. In infants with jaundice, bilirubin crystals are found in the serous cavities, especially the pericardium, the peritoneum and less in amount in the subdural and pleural cavities. It was primarily the histiocytes which carried the crystals. The kidneys were apparently unable to eliminate the bilirubin occurring in icterus neonatorum, since bilirubin was not found in the urinary secretion.

In a series of cholesterol determinations in the blood of mothers and their infants, the content was found to be much higher in the mothers, according to H. Hinglais and J. Govaerts (Gynec. et obst. 22:137 (Aug.) 1930). In infants there was a rise in the amount of cholesterol in the blood during the first few days of life. When the vernix caseosa was allowed to remain on for a longer time than usual, the cholesterol rose in the blood stream and there was a decrease in the bilirubin.

Whether there is any relationship between the high bilirubin and the low cholesterol content in the blood during the first few days was difficult to say, but it was a constant observation that the 2 were never low or high at the same time in any patient. The greater the cholesterol concentration in the blood, the less was the tendency toward hemolysis of the blood. The source of cholesterol is not known but there appeared to be large amounts of it in the suprarenal glands of newly-born in-

fants and it was suggested that these glands might be instrumental in the formation of cholesterol

**Prophylaxis.**—As a means of prevention of icterus neonatorum, liver has been given to women during the last few weeks of their pregnancy, and the results have been gratifying, according to J Bernheim-Karrer and M Grob (Ztschr f Kinderh 50 672, 1931) To one mother who had had 2 of her previous infants die of severe jaundice conditions, liver was given during the last weeks of pregnancy and her newly-born child, though somewhat icteric, survived and was in good health Subsequently, other pregnant women, especially those with a considerable degree of anemia were given liver during the last weeks of gestation It was observed that icterus neonatorum occurred less frequently and was milder than in a control group The reason for the success of this treatment had not been discovered

Familial jaundice, defined as a disease occurring in certain families and present in several consecutive pregnancies, was observed in 2 infants, fatal in both, by W L Buhrman and H N Sanford (Am J Dis Child 41:225 (Feb) 1931). These infants had considerable jaundice at birth, together with large livers and spleens There was definite anemia and a large number of nucleated red blood corpuscles present in the blood The van den Bergh test gave an indirect reaction. The stools were dark in color; the urine contained bile pigments One patient died on the fourth day, the other on the second day after birth. At necropsy, there was hyperplasia of the bone-marrow and the presence of blood-forming islands in the liver, but no evidence of infection or congenital anomaly From the findings,

the lesion was thought to have resulted from an abnormal destruction of red corpuscles Whether the etiology of this condition rests with abnormalities of the liver, the spleen, the reticulo-endothelial system, or of the red corpuscles themselves was difficult to determine The presence of blood islands in the liver suggested the incomplete involution of a fetal structure

**ASPHYXIA.—Treatment.**—In order to determine the necessity of administration of carbon dioxide to infants with asphyxia, H F Kane and J Kreiselman (Am J Obst and Gynec 20 826 (Dec) 1930) made determinations of the CO<sub>2</sub> content of blood of the cord in newly-born infants In those who did not breathe at all, the CO<sub>2</sub> content averaged 54.6 per cent In those who breathed only once or twice while the blood was being taken, the CO<sub>2</sub> content averaged 47.3 per cent In infants crying shortly after birth, the CO<sub>2</sub> was 44.9 per cent Since the CO<sub>2</sub> is normally high in concentration in newly-born infants' blood, and even higher in those with asphyxia, the treatment with CO<sub>2</sub> inhalation was thought to be of no avail as a method of resuscitation or as a stimulus to respiration

However, in the opinion of Y Henderson (J A M A 96 495 (Feb 14) 1931), the only physiologic method of stimulating the respiratory center is by a sufficient CO<sub>2</sub> concentration Even in infants with asphyxia who have abnormally high CO<sub>2</sub> concentrations in the blood, the respiratory center may be considered as asphyxiated also and requiring still greater CO<sub>2</sub> concentrations to stimulate it Besides the asphyxia of the newborn, there are a certain number of infants who breathe from the time of birth, but who have incompletely expanded lungs, and are liable to have sub-

sequent attacks of asphyxia and may also develop pneumonia. Such infants should likewise be treated with resuscitation methods to prevent these complications. Henderson advises the use of an **apparatus** he had described in detail previously, which consists of a mask which fits over the head of the infant. To the mask is connected a bag containing **carbon dioxide** and **oxygen**, the former in about a 10 per cent concentration. Alternate pressure on the chest of the infant and on the gas bag creates a flow of air in and out of the lungs.

The use of the **Drinker respiratory apparatus** for the treatment of 5 infants with marked asphyxia neonatorum was reported by D. P. Murphy and J. A. Coyne (J. A. M. A. 95. 335 (Aug 2) 1930). Each infant had been made to take a few breaths by mechanical means of stimulation but none were breathing when placed in the respirator. Within about  $\frac{1}{2}$  to 2 hours the infants had begun rhythmic breathing and 2 infants survived. The apparatus had many practical advantages in that it greatly improved the rate and rhythm of respiration, it kept the patient at constant warm temperature, allowed for changes in position and the feeding of the infant without disturbing the respiration.

The usefulness of the **Drinker apparatus** has been extended to patients with numerous other types of illness. The instrument as first devised (1929) was intended primarily for the treatment of persons with poliomyelitis who were suffering from respiratory paralysis. In a subsequent report, P. Drinker, T. J. Shaughnessy and D. P. Murphy (J. A. M. A. 95. 1249 (Oct 25) 1930) mention its value in the treatment of patients with *gas poisoning*, *alcoholic*

*coma*, *drug poisoning* (especially *morphine*), *drowning*, *postoperative respiratory failure* and *asphyxiation of the newborn*. For infants and younger children a small model of the apparatus, similar in design to the adult machine, was constructed.

D. P. Murphy, J. E. Bowman and R. B. Wilson (Am. J. Dis. Child 42. 1075 (Nov.) 1931) employed the **Drinker respiratory apparatus** in the treatment of 3 immature infants having respiratory difficulties. Two of these patients were prematurely born and the third was the smaller of twins. These patients had attacks of cyanosis and apnea, a type of respiration which was irregular in rate and in depth, and which periodically would grow weaker and finally cease for a time. At the appearance of cyanosis the infants were placed in the apparatus and the rhythmic negative pressure of 8 to 10 cm. was applied at the rate of 45 times a minute. The infants responded well and 2 recovered completely. The third died during a period of apnea before it could be placed again in the respiratory apparatus. These patients, unlike older children and adults who had been treated with this method, never continued the respiratory rate set by the apparatus after the treatment was stopped, but they assumed their own individual rates and rhythms. The advantages of the Drinker machine for maintaining respiration were considered to be its ease of control, the possibility of maintaining the patient in a warm environment, and in keeping up the treatment for long periods of time.

The same authors report the results of the use of the **Drinker apparatus** in 35 newly-born infants (Am. J. Obst. and Gynec. 21. 528 (Apr.) 1931). These patients had difficulties of res-

piration immediately after birth. Of the entire group, 21 survived and, although it was difficult to determine what part this treatment played in their recovery, it was felt that certain ones, at least, would have died without it. Of the 14 infants who died, the majority were found to have had some intracranial lesion or were premature, in which case the mechanical respiratory treatment would have no avail.

**PREMATURITY.**—The *mental development* of children who had been born prematurely was studied by G. J. Mohr and P. Bartelme (*Am J Dis Child* 40:1000 (Nov) 1930). A group of 113 such patients were given mental tests at the ages of 8 months to 7 years and compared with a group of 40 patients who had been born at full term. The Gesell performance tests and the Kuhlmann Binet tests were employed. According to the former type of tests, 43 per cent of the premature group were of average intelligence, 35 per cent were below average, and 22 per cent above. According to the Kuhlmann Binet tests, 40 per cent were average, 40 per cent above average, and 20 per cent below, including 3 obviously mentally defective infants. In the control group there were more children with average intelligence and less variation above or below. The prematurely-born infants did not differ from the control group in the time of teething, walking and talking or bladder control, providing due allowance was made and the weeks of prematurity were added to their age. Those infants who were considerably underweight were somewhat behind the others in these achievements. Of the 113 premature infants, 28 had had symptoms of intracranial hemorrhage at birth, but of the latter group only 3 were mentally retarded. On the

other hand, 7 infants with no previous symptoms of hemorrhage, later had signs of physical abnormality, such as spasticity. The conclusion was that infants born prematurely, but who survived, did not suffer more from hemorrhage and birth injury than did full-term infants.

A group of 559 premature infants who had reached the ages of 6 to 21 years were examined in regard to their mentality by A. Sunde (*Acta obst et gynec. Scandinav.* 9:477, 1930). Seven per cent of them were found to be mentally defective and 57 per cent were definitely feeble-minded. As a group, the prematurely-born had not developed mentally as well as normal children.

(For further discussion of the effect of intracranial injury on mentality, see section on Feeble-mindedness in Children.)

A study of the *respiration* of 9 premature infants was made by L. A. Shaw and F. R. Hopkins (*Am J. Dis Child* 42:335 (Aug) 1931). An apparatus was constructed to record graphically the rate and volume of respiration. The rate was found to vary from 36 to 87 a minute in the different infants, while in the same patients the rate would sometimes vary from 50 to 90 per cent from minute to minute. There were also considerable differences of volume intake, from 121 to 323 cc per minute per pound of body weight. When observed for 30 consecutive minutes the respiratory volume of a single patient sometimes varied from 45 to 55 per cent. These measurements were always taken on quiet infants. It was thought that the wide differences of respiratory volume did not lead to hyperventilation because a considerable amount of air did not reach far into the



lungs but remained in the "dead spaces." The possibility of a variable metabolic rate in the same infant from day to day might explain partially the variation of respiratory volume.

**Treatment.**—A new apparatus for maintaining constant *body temperatures* of premature infants has been devised by R. M. Tyson and E. F. Burt (Am J Dis Child 39 321 (Feb) 1930). Three objections to the average incubator now used for this purpose are: (1) it is not the temperature of the infant but the air in the structure which is kept at a normal degree of heat; (2) the heat required by infants in different seasons of the year varies, and (3) during the care and treatment of the patient considerable chilling can take place. In the new device, a special thermometer is strapped in place in the axilla of the infant and attached to an automatic controller which turns on the heat in the electric pad on the top of the chamber when the infant's temperature falls below 97° F (36.1° C) and turns off the current when it reaches 98° F (36.7° C). Adjustments for higher or lower temperatures may be made. A recording device charts the temperature variations. Although the apparatus has not been tested in a large series of patients, its advantages of simplicity and effectiveness have encouraged the inventors to report its construction. It is an ingenious device that marks a distinct advance over the older incubator.

On the assumption that premature infants do not have properly functioning glands of *internal secretion*, E. Schultze (Munchen. med. Wchnschr. 77 1100 (June 27) 1930) gave them intramuscular injections of **pituitary gland substance (anterior lobe)**. The infants made rapid gains in weight following the treatment.

**THYMUS GLAND ENLARGEMENT.**—**Diagnosis.**—In an x-ray study of thymus shadows of newly-born infants H. B. Podlasky and S. F. Kohn (Am J Dis Child 39 782 (Apr) 1930) were unable to demonstrate a correlation between the size of the gland and symptoms of tracheal compression. The series consisted of 100 infants and the x-rays were taken with a constant technic, although the phase of respiration differed somewhat at the time of exposure of the plates. Thirty-five infants had definitely enlarged thymuses but none had the usual symptoms attributed to an enlargement. Cyanosis was present temporarily in 2 patients and 1 other had a slight stridor, but in no instance did these 2 symptoms occur simultaneously and all the patients remained in good health. Large well-nourished infants were thought to have had larger thymic shadows as a general rule than the normal or underweight infants.

X-ray examination of 50 newly-born infants was made on the second and twelfth day of life, by E. P. Pendergrass and E. S. Thorpe, Jr (Am. J. Dis Child 40 1370 (Dec) 1930). Only 2 infants of the group had such thymic enlargement that the trachea was displaced and the lumen diminished in size, but they had no symptoms of this condition and, although no treatment was given, these findings disappeared within 6 to 8 weeks. On the other hand, 32 infants of the group had symptoms of stridor and respiratory difficulty, yet none of them showed thymic enlargement.

A. C. Singleton (Canad M. A. J 22: 23 (Jan) 1930) made a x-ray examination of 95 newly-born infants, employing a constant technic. Any shadow of the thymic region greater than 3.5 cm.

was considered as denoting an enlargement of the gland. In his series, 35 infants had definite enlargement. In his opinion, any child with either an enlargement such as this or with thymic symptoms should be given radiation treatment.

Routine x-ray examination of newly-born infants frequently reveals other anomalies of one sort or another and, according to C. H. Davis and G. W. Stevens (Am J Obst and Gynec 20 73 (July) 1930), it should be a routine procedure. In a group of 702 infants examined by the x-ray, 55 per cent. were found to have some abnormality, 32.6 per cent. had large thymic shadows, 26 per cent. had abnormal lung conditions, including 1 per cent. with spontaneous pneumothoracies. An abnormal appearance of the heart shadow was noted in 15 per cent. of this series which included variations of size, shape and position. The symptoms of enlargement of the thymus gland may be confused with certain other types of lesions affecting respiration. Two congenital lesions with such symptoms have been reported recently. One of these is congenital inspiratory stridor which was observed in 7 newly-born infants by C. Bagg (Monatschr f Kinderh 45:102 (Oct) 1929). Laryngospasm, which frequently causes this symptom of stridor, did not occur in this series, but 2 had malformations of the epiglottis; 2 had malformations of the lower jaw; 1 had a very large tongue, 1 had a large thyroid; and 1 had a large thymus gland. It was evident that the symptom of stridor may occur in several conditions and the treatment of each patient must be directed towards its specific etiology.

Hypoplasia of the mandible as an etiologic factor in causing difficulty of

breathing and attacks of cyanosis has not been given sufficient attention, according to R. C. Eley and S. Farber (Am J Dis Child 39 1167 (June) 1930). They observed 4 infants with small receding mandibles who had difficulties of respiration, probably because of the tongue falling back into the pharynx and obstructing the breathing passages. Other deformities of the mouth and palate may have contributed to the difficulty; for instance, all the infants had a cleft palate. For treatment, a **metal support** was strapped under the jaw and supported by a band around the head. This tended to displace the jaw forward and upward and proved very helpful in alleviating the symptoms of cyanosis and choking. In less marked deformities, **postural treatment** alone sufficed which usually consisted of placing the infant on its face and elevating the foot of the bed.

**OTHER DISEASES OF THE NEWBORN.**—A *pemphigus* infection of 65 infants in a maternity hospital was reported by F. C. Neff (Arch Pediat 46 24 (Jan) 1929). The disease seemed to be highly infectious in nature in that it readily spread from one infant to another, especially when several infants were brought in close contact with each other during bathing periods. It may possibly have been transferred by a third person, such as an attendant or nurse. Treatment with ammoniated mercury ointment, mercurochrome or gentian violet had but little curative value. An alcoholic solution of brilliant green and crystal violet (**Milian's solution**) was more effective in treatment, but, *prophylaxis*, by means of **isolation**, was the most essential phase of care. The infection is supposedly due to a *Staphylococcus aureus* but frequently other microorganisms in-

vade the lesions and in this series 1 death had been caused by septic complications.

Careful routine examination of the eyes of newly-born infants frequently discloses ocular lesions, requiring early treatment, according to M. W. Jacobs (New York State J. Med. 30: 1355 (Nov. 15) 1930), who urges this useful diagnostic procedure. *Nerve injuries, corneal damage and lacerations of the lids*, may result from trauma at birth, from long difficult labor, or from disease, especially syphilis. By the ophthalmoscopic examination of the fundi certain intracranial lesions may be suspected, though not always definitely diagnosed by this procedure alone. *Retinal hemorrhages* were present in 12 per cent. of a series observed by the author. This lesion tends to clear up and 13 children with this condition at birth failed to show it at the ages of  $3\frac{1}{2}$  to  $5\frac{1}{2}$  years. The trauma of instrumental deliveries was thought to be the most common cause of retinal hemorrhage.

In an attempt to combat *inanition fever* of newly-born infants together

with the loss of weight and what was considered to be an acidosis due to the dehydration and frequent vomiting, **sodium citrate** in addition to a **lactose solution** was given by H. L. Eder and B. Bakewell (Am. J. Dis. Child. 42: 1079 (Nov.) 1931). To 100 infants, 2 ounces (60 Gm.) of a 5 per cent lactose solution were given every 4 hours for the first few days of life. To another group of 100 infants every 2 ounces (60 Gm.) of the lactose solution were supplemented by 5 grains (0.3 Gm.) of sodium citrate. The series of patients receiving the latter solution suffered less from the customary loss of weight of the first days of life, regained their weight readily, and only 3 per cent. had inanition fever. In general, these infants were more active, had a better color, and were more free from icterus neonatorum than the control group who received no sodium citrate.

**NIRVANOL.** See CHOREA MINOR. TREATMENT.

**NITROUS OXIDE.** See ANESTHESIA.

## O

**OBESITY.—ETIOLOGY.**—A perusal of the literature on obesity in 1931 shows that there are 2 distinct schools of thought in regard to the cause and treatment of this condition. The continental writers, particularly those quoted later in this article, consider that all cases of obesity have a large endocrine element in their etiology. The majority of American and English writers, on the other hand, feel that aside from the classical types of endocrine obesity (*adiposis dolorosa*, *pituitary obesity*, *eunuchoid obesity*, etc.),

the ductless glands play very little part in the production of the obesity and it would seem that the latter group has presented the more logical proof for their stand.

The diagnosis of "endocrine imbalance" is too frequently made not only in obesity but other medical conditions. Unfortunately, methods of precision in the diagnosis of disturbances of one or more of these ductless glands are few, but it does seem that unless definite laboratory proof can be obtained or a distinct clinical entity recog-

nized, the label "endocrine" should be used with hesitation

D M. Dunlop and R M M Lyons (Edinburgh M J 38 561 (Oct ) 1931) report a carefully studied series of 523 cases of obesity and feel that the division into an endogenous and exogenous classification is impossible in the great majority of cases In their series, 82 per cent were definitely endogenous, 37.2 per cent were probably exogenous, while 53.6 per cent were of a mixed type. They found that heredity was a most important etiological factor, 69.2 per cent having had obese parents, while 45 per cent. were large carbohydrate eaters Contrary to expectation, 59.7 per cent of patients claimed to be of excitable dispositions; only 10.4 per cent phlegmatic They found a high incidence of gall-bladder disease among the group. On discontinuing the treatment there is a tendency to gain weight slowly The greater the original weight and the more rapid the loss under treatment, the greater was the tendency to regain weight on discontinuing the diet They treated these cases mostly by diet, although thyroid was occasionally used as an auxiliary

There is only one basic cause for obesity, in the opinion of L. H. Newburgh (J A. M. A. 97:1659 (Dec. 5) 1931), *i e*, invariably the result of *over-eating*. The available energy of the diet exceeds the transformation of energy on the part of the individual. He feels that obese individuals disregard the primitive stimulation of a satisfied appetite and that this instinct becomes dulled and notifies its host too late that the body needs are satisfied He cites studies in confirmation of this opinion that show the dominant position of appetite in establishing the body weight and the fact that many obese in-

dividuals have emotional and unstable personalities, and that during times of nervous stress they obtain release by nibbling of food

The author has been able in his study to carefully determine (1) how much energy the subject receives in his diet, (2) that the diet was strictly adhered to, and (3) to obtain the transformation of energy for the whole period of observation From such data he could readily calculate the amount of tissue actually being destroyed and plot the weight loss caused by such oxidation In many cases the actual loss of weight did not correspond to the anticipated loss. This, he feels, is due to a change in the water balance and he has demonstrated that actually a gain in weight might take place while the patient is losing body tissue; he has been able to reproduce this phenomenon by under-feeding the subject in such a way that a rapid destruction of the liver glycogen is brought about The reverse might be true also, for the patient might actually lose weight while being over-fed because of the loss of water He feels, as do Evans and Strang, that this factor must be understood and taken into consideration in treating cases of obesity, but that it tends to correct itself over a period of some weeks It does, however, explain some of the disappointments of the failure to lose weight even on a carefully measured and restricted diet

Neither Newburgh or Evans, who have done a large amount of work on the water balance, feel that it is of enough importance to use diuretics to aid the excretion of fluids.

C. W. Nissler, En Shui Tai and Burgess Gordon (New York State Med. 31:887 (July 15) 1931) state that in the beginning the potential obese patient

eats excessively because of pleasure and example. This is followed by an acceleration in the production of insulin, which further influences the patient to increase the intake of carbohydrates. The result is a step-up in the output of insulin. Less physical work is attempted because exercise induces hyperglycemic-like phenomena. The ultimate effect is lassitude and the accumulation of unused fuel in the form of fat. If this is true, a decrease in the function of various glands may be the result rather than the cause of obesity. The patients are required to carefully tabulate their daily food intake at meal time and between meals. When this is obtained the carbohydrate is cut two-thirds. No change is made in the protein, fat or water. In order to relieve hunger, 2 to 4 Gm (30 to 60 grains) of dextrose, as flavored tablets, are administered every half-hour between meals, adding 20 to 40 Gm ( $\frac{2}{3}$  to  $1\frac{1}{3}$  ounces) of dextrose to the diet. By relieving the patients of the periods of hyperglycemia, they feel they have been able to reduce hunger and gain cooperation in the diet régime.

From studies made by G. Kahlmeter (*Acta med. Scandinav.* 75:107 (Apr. 28) 1931) he concluded that in certain cases of obesity the salt and water excretion is a fault probably due to derangement of the sympathetic system or of certain endocrine glands. He emphasized the clinical value of recognizing this type of obesity and of the importance of salt restriction. Many workers here and abroad feel that this is important in a certain type of refractory case and even advise the use of diuretics such as **theophylline**. The **salt restriction** has the additional advantage that it renders the food less attractive to the palate.

**PATHOLOGICAL PHYSIOLOGY.**—In discussing the subject of obesity and leanness, Hugo R. Rony (*Illinois M. J.* 59:302 (Apr. 1931)) feels, as do some of the other workers, that the basal metabolic rate should be calculated by normal height and weight of the individual, rather than actual height and weight, and by so doing has found, as has Strange and others, that the majority of obese individuals show an increased rate by such calculation. This he has found to amount to about plus 30 per cent for each 100 pounds above the "ideal" weight and for this he proposes the term "basal metabolic ratio."

Regarding the question as to why obese persons have a higher basal metabolism relatively, the following considerations are suggested. Some part of the excess basal metabolism of the obese may be accounted for as the metabolism in the excess fat tissue; but this part can account for but a fraction of the basal metabolic ratio. It is seen from this work that 100 pounds overweight is usually associated with basal metabolic ratios around plus 30 per cent. If all of this excess were due to metabolic activity in the excess fat tissue, this fat tissue would be from  $\frac{1}{3}$  to  $\frac{1}{2}$  as active metabolically as the rest of the body. This is hardly conceivable. Undoubtedly, some tissues developed along with the excess fat of the obese, such as additional interstitial tissue, vessels, skin and subcutis, may be metabolically quite active and even the mass of fat cells proper may have, at least at times, some metabolic activity, but it is probably safe to say that the larger part of the observed excess basal metabolism cannot have its origin in the excess tissues.

If it is considered that an obese person is composed of excess fat tissue

and basic tissues, it must be concluded from the above that the larger portion of the excess metabolism originates from the basic tissues as an actual increase in their normal metabolic activity. All or only some parts of the basic tissue mass may be involved. Thus the work of the heart is evidently increased in the obese, even at complete rest. And the respiratory movements of the heavier chest require additional energy production in the respiratory muscles; furthermore, obese persons are frequently dyspneic, which necessitates increased work of the respiratory muscles, even at complete rest, and some may even be orthopneic. This extra activity of the heart and the respiratory muscles can easily account for from 5 to 10 per cent. in the basal metabolic ratio of the obese.

Another factor which may contribute more or less heavily to the positive basal metabolic ratio of the obese, representing an increased metabolism in all basic tissues, is the effect of the so-called "luxus consumption." Grafe and his collaborators proved that prolonged overfeeding increased the basal metabolism of most persons, the increase being called "luxus consumption." The increase of the basal metabolism brought about by previous overfeeding is, according to Grafe, less marked in obese than in normal persons, but even so, it may be responsible for some portion of the high basal metabolic ratio in obesity, considering that many obese persons are in a state of chronic overfeeding. This factor may possibly account for as much as 20 per cent. in the value of the basal metabolic ratio of certain obese persons.

In other cases the high basal metabolic ratio may be due to increased metabolism in all of the protoplasmic structures because of overactivity of the

thyroid gland. Obesity and hyperthyroidism are by no means incompatible, as has been reported by others.

The author also discusses the effect of an altered specific dynamic factor of foods, but feels that he was able to demonstrate no ratio from normal in the obese. The question of muscular activity, particularly the rôle played by "specific dynamic after-effect of muscular activity" has been considered, although there is very little experimental work to exploit such hypotheses nor does Rony feel the balance between the caloric intake and output to be of such importance as other investigators have believed.

These facts and certain clinical observations necessitate a revision of the present conception of obesity, according to this author. The chief points of this new conception are. In normal persons the body fat content is automatically maintained by a regulatory mechanism which is adjusted to a threshold represented by the normal fat content of the tissues. In obesity and leanness this regulatory mechanism operates with normal efficiency, only it is adjusted to an abnormally high fat threshold in obesity, and to an abnormally low fat threshold in leanness. Obesity is not synonymous with excess weight, obesity may be present without excess fat content, and *vice versa*. It is necessary to distinguish between the "dynamic" stage and the "static" stage of obesity. In the dynamic stage one or several factors of the caloric equilibrium are of abnormal value, and the caloric balance is necessarily disturbed. In the static stage all caloric factors may be of normal value, and the caloric intake and output are balanced. Anomalies of caloric intake or output in obesity or leanness have no basic etiologic im-



portance, they are merely means used by the disturbed body fat regulatory mechanism to insure establishment of an "abnormal level." Accordingly, the study of the caloric metabolism, although of value, will not solve the question of the basic causes of obesity. Human obesity is basically endogenous, but the underlying disturbance of the fat content regulating mechanism may be aggravated or improved to a certain extent by exogenous factors.

**COMPLICATIONS.**—S H Proger (Arch Int Med 47 64 (Jan) 1931) has investigated the *electrocardiographic changes* taking place in obese individuals. He points out the fact that the electrocardiogram undergoes certain changes when the position of the heart in the chest is altered, and stresses the point that there is a rather definite relation between the anatomic angle of the heart as measured on the x-ray and the electrical angle as derived from the electrocardiogram. In other words, as the position of the heart becomes more transverse, the electrocardiogram shows a gradually increasing left axis deviation, and as the position becomes more vertical, the axis deviation tends to change to the right.

He felt that on the basis of these observations it seems logical that in obese people, in whom the diaphragm is usually pushed up so that the heart lies in a comparatively transverse position, there would be a tendency to the production of left axis deviation, as measured by the Q R S-wave and of associated changes in the T-wave.

In the present study the cases were separated into 2 groups. (1) those cases of obesity in which the heart was considered normal, and (2) those cases showing hypertension (a systolic blood-pressure of more than 170 mm. of

mercury), x-ray evidence of cardiac enlargement or other cardiac abnormalities. One hundred cases were studied. The electrocardiograms were taken with the patient in the sitting position, with tight clothing loosened, as Romberg has shown that tight corsets may definitely change the position of the heart. Orthodiagrams were made in the erect position within 1 week of the electrocardiographic examination. The diagnosis of cardiac enlargement was based on these orthodiagraphic observations, Otten's tables being used as standards. From the orthodiagram the anatomic angle of the heart was obtained and compared with the electrical angle calculated according to Einthoven from the electrocardiogram. The anatomic angle was taken as that angle which is formed by a horizontal line and a line drawn from the junction of the curve of the right auricle in the orthodiagram with that of the superior vena cava to the apex of the heart. The approximate duration of the obesity, as well as the percentage of overweight according to the standard tables of the Metropolitan Life Insurance Company, were both recorded as being of possible significance.

**Analysis of Cases.**—*Uncomplicated Obesity.*—Those cases are considered uncomplicated or cases of simple obesity in which the physical examination of the heart gives negative results, the orthodiagram shows no enlargement or abnormal contour, and the blood-pressure is not elevated. Fifty-five are included in this group.

Of these 55, 39 (71 per cent) appeared on simple inspection to have some degree of left axis deviation, *i.e.*, exaggeration of the R-wave in Lead I and the S-wave in Lead III. By actual measurement of the index and angle, it

was found that 31 (56 per cent) showed definite evidence of left axis deviation (angle below 0 degrees or index above +20). In 40 of the 55 cases the electrical angle was below 20 degrees and in 28 it was below 0 degrees, which is taken by many as the lower limit of normal. Thirty-two of the 55 showed an index over +15, and 20 (36 per cent) showed an index of over +20, which is considered by White to indicate definite left axis deviation. This high incidence (36 per cent.) of axis deviation beyond plus 20 in cases of simple obesity is a distinct contrast to the 0.5 per cent. incidence of such an axis in 1812 adults without disease of the heart reported by Ferguson and O'Connell. The average angle of the entire group was 7 degrees; the average index, plus 16.

Thirty-nine of the 50 cases showed an inverted T-wave in Lead III, and twenty-four exhibited changes in the P-wave in Lead III (flat or inverted). In studying the electrocardiograms showing inversion of T3 an interesting correlation was observed. It appeared that inversion of T3 was a fairly constant concomitant of left axis deviation when the deviation was thought to be due to change in position. Twenty-eight of them showed an inversion of T3. In order to test the validity of this observation, the author reviewed the records of 31 persons of average size who showed left axis deviation associated with hypertension (systolic blood-pressure over 170 mm of mercury) and x-ray evidence of cardiac enlargement. Cases showing inversion of the T-wave in Lead I or II or abnormal spreading of the QRS complex were not included. Only 6 of these 31 showed an inversion of the T-wave in Lead III (in 6 of the cases T3 was iso-electric and in 19

erect), in contradistinction to 28 of 31 in the former group. In the latter group, cases clinically associated with left ventricular hypertrophy are being dealt with, so that it is reasonable to suppose that in this group the axis deviation in most of the cases is the direct result of the hypertrophy. The figures then indicate that left axis deviation due to change in position is usually associated with inversion of the T-wave in Lead III, whereas left axis deviation due to relative left ventricular hypertrophy is commonly associated with an erect T-wave in Lead III.

There was no significant change in the T-wave in Leads I and II in any of the cases of simple obesity, even though the axis deviation was considerable in a fair percentage of the cases. This is interesting because, as Cohn has shown, in the production of axis deviation experimentally by rotating the leads around a large triangle laid out on the chest, thus simulating rotation of the heart on its A-P axis, the T-waves change with the QRS-waves, and as the QRS-waves become inverted and deepen, the T-waves also become inverted. Experimentally, this occurs in all of the leads. White expressed the belief that although inversion of the T-wave in Lead I or in Leads I and II does not occur in a normal heart, it may be the result of marked left axis deviation without disease of the coronary arteries or bundle-branch. Such left axis deviation with inversion of the T-waves in Lead I or II has been found by White to be associated with left ventricular hypertrophy and dilatation (with extension of the bundle-branch as well as increase in muscle mass). If with only slight left axis deviation the T-wave is inverted in Lead I or II, White held that some other factor, such as blocking the

left bundle-branch, cardiac infarction or myxedema is present. In this study only in Lead III did the T-wave become inverted as a result of the deviation.

*Obesity with Complications*—There were 40 cases of obesity with cardiac complications and 5 cases with essential hypertension without demonstrable cardiac involvement. Twenty patients had hypertension and cardiac enlargement. Thirteen of these (65 per cent) showed an angle of less than 0 degrees or an index over plus 20 (definite left axis deviation). The average angle was 6 degrees; the average index, plus 21. Only 5 of this group showed inversion of the T-wave in Lead III, while 3 showed inversion of the T-wave in Leads I and II, and one inversion of the T-wave in Lead I alone. Four showed P-wave changes in Lead III. There were 5 cases of hypertension without cardiac enlargement. Of these, 3 showed left axis deviation, 2, inversion of the T- and P-waves in Lead III, and 1, inversion of only the T-wave in Lead III. There were 19 cases of enlargement that appeared on the orthodiagram to be chiefly left ventricular, but without hypertension at the time the picture was taken. Of these, 11 showed left axis deviation, 10 inversion of T3, and 7 changes in P3. The average angle of this group was 8 degrees; the average index, plus 19. There was 1 case of rheumatic mitral stenosis that showed a normal angle and index, but in which a diphasic T-wave in Lead II and an inverted T-wave in Lead III were recorded. The orthodiagram in this case showed a distinct right-sided enlargement.

The electrical axis did not differ materially whether or not the heart was involved. For example, the average

angle in the group with simple obesity was 7 degrees and the average index plus 17, while in the group with hypertension and cardiac hypertrophy the averages were 6 degrees and plus 21, respectively. Fifty-six per cent of the cases of simple obesity showed definite left axis deviation, while 65 per cent of the cases of obesity with hypertension and cardiac hypertrophy showed such an axis. It is known that in people of ordinary size there is a definitely greater incidence of left axis deviation in those with hypertension and cardiac hypertrophy than in those with no cardiac abnormalities, so that axis deviation is considered by many to be of some value in the diagnosis of relative ventricular hypertrophy. In the obese, however, left axis deviation appears almost to the same degree and as frequently in cases of simple obesity as in cases with hypertension and cardiac hypertrophy. Thus changes in the axis that may be produced by left ventricular hypertrophy are obscured by the changes associated with obesity. Therefore, deviation of the axis is probably of no significance in the obese. Although inversions of the T-wave in Leads I and II theoretically may be associated with marked deviations in the electrical axis, in this study they are found not to occur in those cases in which the heart is apparently normal, despite marked deviation of the axis. In the 4 cases in which these inversions were associated with marked left axis deviation, there is definite clinical evidence of myocardial disease.

*Comparison of Electrical and Anatomic Angle*—Since it is true that the changes in the electrocardiogram of the obese seem to be due to the changes in position resulting from the obesity rather than to any direct cardiac effect,

it appeared advisable to compare the anatomic and electrical angles and to determine if possible whether or not the usual transverse position of the heart in obesity, with its low anatomic angle, is paralleled by changes in the electrical angle

There does appear to be a general relationship between the anatomic angle of the heart as measured with a protractor on the orthodiagram and the electrical angle as calculated from the electrocardiogram. Of the 25 cases in the entire group in which the anatomic angle was below 30 degrees and in which the heart may be said to have been in a more or less transverse position, the average electrical angle was 1 degree, which may reasonably be considered as left axis deviation. Of 11 cases in which the heart was more oblique, the anatomic angle being over 40 degrees, the average electrical angle was 28 degrees, which may be considered normal. A similar comparison in the group with normal hearts shows that the average electrical angle was 1 degree in those cases in which the anatomic angle was below 30 degrees, while it was 20 degrees in those cases in which the anatomic angle was above 40 degrees. In the group with simple obesity there were 32 cases with the anatomic angle below 35 degrees. The average electrical angle of these cases was 2 degrees, the electrical angle in none being over 25 degrees. There were 23 cases of simple obesity in which the anatomic angle was more than 34 degrees (from 35 degrees to 47 degrees). The average electrical angle in this group was 17 degrees, and only 2 cases showed an electrical angle below 0 degrees or definite left axis deviation. It is fair to conclude from these figures that the variations in the anatomic angle

that occur with rotation of the heart on a horizontal axis usually are associated with corresponding changes in the electrical angle of the heart. The important influence on the electrocardiogram of rotation of the heart on a vertical axis, which cannot be ascertained in a study such as this, may well account for the discrepancies noted.

*Influence of Age, Sex, Percentage of Overweight and Duration of Obesity*—The average percentage of overweight was 33. The percentage of overweight beyond approximately 25 in the individual cases seemed to have no direct bearing on the electrocardiographic changes. The age was likewise found to have no effect in the cases studied, in which all of the patients were adults. For example, in the 22 cases of simple obesity in persons between the ages of 20 and 40, the average angle was 7 degrees and the average index plus 15; while in 30 cases of simple obesity in persons between the ages from 40 to 60, the average angle was 8 degrees and the average index plus 16. The duration of the obesity was in no way related to variations in the electrocardiogram in the normal group, nor did the sex appear to be an influencing factor.

**TREATMENT.**—*Endocrine Therapy.*—As stated earlier there have been many articles written abroad which advocate the almost routine use of thyroid preparation in obesity with subnormal basal metabolic rates.

Schittenhelm and Eisler (Klin. Wchnschr. 10.673, 1931) state that they believe in the majority of cases of obesity an underlying metabolic disturbance is at fault, principally thyroid, and that attempts to reduce the weight of a person by reducing the calories is, therefore, not sufficient in most cases, since this does not control the cause but merely

the result, *i.e.*, obesity. On the basis of the study of 100 cases they feel that the majority of cases can be successfully treated by **thyroxin** and **diet**. If the main object is to reduce the weight rapidly, they administered large doses of thyroxin by mouth and intravenously. If, however, the hormonal-nervous equilibrium is to be influenced, the thyroxin is given orally and in smaller quantities. The writers recognize that continued thyroxin administration may produce thyrotoxicosis and suggest, in order to avoid this, that the size of the dose be varied and the patients be given a thyroxin-free day. Unfortunately, no data is given on the basal metabolic rate of these patients, nor is there any record of a "follow-up" to determine the later results of such intensive thyroid therapy, which would, if the conclusion of Evans and Strang cited above were true, be apt to further embarrass an already overstimulated thyroid.

Owing to the divergent views held as to the advisability of the use of **thyroxin** in obesity, A. Hellfors (Munch med Wchnschr 78 826 (May 15) 1931) investigated 25 cases. These were refractory to dietary management and had lowered basal metabolic rates (whether it was calculated from the actual or ideal weight the author does not state). The dose administered was 0.5 mg ( $\frac{1}{120}$  gram) by mouth, 3 times a day. This was increased to 5 or 6 times a day, depending on the effect obtained. Without exception, the patients began to lose weight 2 to 3 days after the initial administration, the basal metabolic rate increased with the decrease in weight. The author feels that thyroxin acts indirectly by stimulating the thyroid and the sympathetic nervous system, as the weight loss started 2 to 3 days after the initial dose and con-

tinued 2 to 3 days after the drug was stopped. Temporary symptoms of hyperthyroidism were noticed in cases in which the dose was large and the first symptoms were usually dissatisfaction and irritability.

Most endocrine preparations, except thyroid, are inactive if given by mouth, possibly due to their destruction by the digestive juices.

E. L. Bortz (M Clin North America 14 1037 (Jan.) 1931) suggests the rather simple procedure of administering alkalis (10 to 15 Gm— $2\frac{1}{2}$  to  $3\frac{3}{4}$  drams—of **sodium bicarbonate**, 15 minutes before the **glandular product** is given. He has treated successfully cases of *ovarian obesity* by administering **ovarian extract** in this manner, together with a low caloric diet.

**Diet.**—F. A. Evans and J. M. Strang (J A M A 97 1063 (Oct. 10) 1931) point out that the excess weight in obesity is fat, which is stored as inert tissue, and that this additional weight should not be considered in computing the basal metabolic rate. They calculated this according to the ideal weight of the patient and find that the majority of the obese have an increased basal metabolic rate for their ideal weight, which these observers feel indicates the amount of additional work they must do for being obese. From these studies Evans and Strang conclude that the daily output of these patients is dangerously high and that the caloric deficit necessary for weight reduction should not be attempted by further increase of this factor by feeding thyroid, but that attention should be focused on an adequate depression of energy intake by limitation of the diet. Quick reduction by dietary measures depends on a caloric intake which is as low as is compatible with health. In considering the proteins

of the diet it must be recognized that these must be adequate to maintain nitrogen equilibrium. One gram (15 grains) of protein per kilogram ( $2\frac{1}{2}$  pounds) of ideal weight is sufficient to accomplish this. A large part of the normal caloric intake is carbohydrate and in a minimum caloric diet this factor must be as low as possible. If, however, the diet consists of protein alone, it is impossible to maintain a nitrogen equilibrium on 1 gram of protein per kilogram of body weight because of the diversion of as much as 60 per cent of the protein for its anti-ketogenic action. They, therefore, allow 0.6 grams (10 grains) of carbohydrate for each gram (15 grains) of protein. No fat was given other than that inseparable from the protein ration. To this was added a daily supply of inorganic salts and vitamins as *viosterol* or milk for the fat soluble vitamins. The other vitamins were supplied by the carbohydrate ration from 5 per cent vegetables with the addition of yeast.

These patients were kept on such a diet yielding 400 to 600 calories per day for 2 or 3 weeks, which means that they lost 1500 to 2500 calories per day by burning their own fat. The weight of fatty tissue which corresponds to such deficits is from 150 to 200 grams (5 to  $6\frac{3}{4}$  ounces) a day. In other words, after a week of rigid dieting the loss of actual body tissue is  $2\frac{1}{2}$  to  $4\frac{1}{4}$  pounds (1134 to 1927 Gm). Any greater loss is due to water shifts.

When the nitrogen equilibrium was established, the total basal caloric requirement was made up by adding an adequate amount of fat, *viz*, 150 to 300 grams (5 to 10 ounces). In spite of the high fat proportion, no acidosis or ketosis was found. The authors have used these low caloric diets in 187 pa-

tients with good results. The patients did not feel weak or hungry, but did report return of vigor and resistance to fatigue. These cases, too, after losing weight, showed a tendency to a reduction of the basal metabolic rate to normal levels. It is also pointed out that the distribution and temporary storage of water is a phenomenon of great importance in understanding the many fluctuations which occur even on a carefully measured diet. In this series 2 per cent failed to lose weight on the above type of diet. In these the basal metabolic rate calculated for their ideal weight was definitely subnormal and they were helped by the addition of thyroid extract.

**ADRENAL CORTICAL OBESITY.**—The problem of obesity, at least what the writers term "adrenal cortical obesity," has been attacked by Harry Koster, M. Goldzieher, W. S. Collens, and A. W. Victor (*Am J Surg* 13: 311 (Aug.) 1931) from the surgical standpoint. They state that it is a well-recognized type of obesity and is due to endocrine imbalance. They feel that this imbalance may be precipitated by an altered activity of one, or any combination, of several glands which include the gonads, the thyroid, the pituitary and the adrenals, and that this obesity is less often recognized and understood than that of any other group.

The obesity of adrenal origin is always associated with a disturbance in the cortex. This disturbance is based on either diffuse cortical hyperplasia or a cortical neoplasm. These pathological changes produce 3 different syndromes, depending upon the age of the individual at the time of their development.

If the lesion occurs during intra-uterine life, there is a disturbance in sexual development, causing hermaphro-



ditism, in a large number of cases. When the pathological changes begin during early infancy, precocious sexual development results. This type is by far more common in the female, and is very often associated with obesity, excepting when the adrenal cortex is the seat of malignant neoplasm. The third type develops during adult life and is accompanied by obesity, changes in the secondary sexual characteristics toward the male line, such as hirsutism, thickening of the skin and changes in the voice. Amenorrhea of variable duration is a concomitant feature. The obesity may reach extraordinary degrees. The fat is generally distributed with an accentuated deposition in the hips, buttocks and abdomen, breasts, thighs and arms. The forearms and legs are frequently singularly free from fat accumulation. The hands and feet are rather small. Related to this third group is the obesity in old women with the growth of hair on the face. Examination of the adrenals in the latter cases invariably reveals the presence of one or several cortical adenomas.

It has been known for some time that the adrenal cortex influences fat metabolism. This relationship has been experimentally demonstrated by the fixation of blood fats in the tissues after injection of interrenin, the specific principle of the adrenal cortex isolated by Goldzieher. These observations have been confirmed by others. Other investigators, by feeding their animals dried adrenal cortex, obtained considerable increase in body weight. McKinlay and Fischer also observed a stimulation in the development of the testicles, while Adler, who fed dried cortical adenoma to tadpoles, obtained premature male sexual development together with rapid growth. Very important are also the

observations of Iscovesco and Freschi, who both saw a rapid growth of hair in rabbits after shaving if they were fed cortical substance.

The relationship of cortical hormone to rat metabolism and the results of the feeding experiments quoted here seem to indicate that a hyperactivity of adrenal cortex may be able to produce pathological fat deposition and may also account for pathological growth of hair. The logical conclusion is that obesity and hirsutism accompanying adrenal cortical hyperplasia or tumor are an expression of cortical hyperfunction. On this basis it is rational to propose similar surgical therapy to that advocated for other hyperfunctioning glands, as for example the thyroid.

**CASE HISTORY.**—The following case is reported. K. B., female, 23 years old, complaining of extreme obesity, was admitted to the Crown Heights Hospital on Sept 27, 1929. She is one of 7 children, all others of whom are perfectly well. There is no history of metabolic disturbance in the family. She began menstruating at the age of 13. She was very irregular, the intervals varying from 2 weeks to 3 months. The flow lasted 7 days, was scanty, and without pain. Her appetite was voracious, she was not constipated, had no nausea, belching or polydipsia. She had a marked frequency of urination and nocturia, often voiding as many as 15 times a night. At 12 she had influenza, at which time she weighed 100 pounds. During convalescence, after "tonic" treatment, she began to gain weight, so that within a year she gained 75 pounds. She continued to gain progressively until on admission (11 years later) she weighed 335 pounds. Of that weight, 125 pounds were gained in the past year. Her

voice became deep, rough and masculine in character. Hair began to appear on her chest, face, abdomen, forearms and legs.

On examination she presented the following findings. A young woman extremely obese, with fat distribution particularly in the region of her abdomen, hips, arms and thighs. There was a marked growth of hair on her face, extremities, breasts and a masculine distribution of pubic hair extending up to the umbilicus. Her voice was deep and her skin thick.

#### LABORATORY FINDINGS.—

Urine specific gravity 1.018, no albumin, no sugar, microscopic negative. Blood count: hemoglobin 85 per cent, red blood corpuscles 5,160,000; white blood corpuscles 8500, polynuclears 78 per cent. Blood-pressure  $105\frac{5}{62}$ , lymphocytes 21 per cent, monocytes 1 per cent. X-ray of skull showed a normal sella turcica. Wassermann test negative, Kahn test negative. Basal metabolic rate, plus 8 per cent. Blood chemistry: sugar 120, creatinine 1.1, urea 10.

**DIAGNOSIS**—A perirenal insufflation of both kidneys was performed with the purpose of visualizing the adrenals by means of the x-ray, but the extreme obesity prevented obtaining a conclusive result.

On the basis of these findings the diagnosis of hyperfunction of the adrenal cortex was made. The differential pathological diagnosis between cortical adenoma and diffuse bilateral hyperplasia, however, was merely speculative and had to wait surgical inspection.

#### SURGICAL TREATMENT.—

The incision extended from the tip of the last right rib to the anterior superior spine, down to the perirenal fat. This

was stripped from the kidney which was then drawn into the lower angle of the wound, covered by a lap sponge and held there by a retractor. The hand was then introduced high into the vault of the exposed area and the fingers found the adrenal gland in the fat. It was easily recognized by its firmer consistency and slightly granular surface. It might be noted here that if any difficulty is experienced in exposing it to view, this is easily obviated by resection of the last rib. A ring clamp placed on the organ helps to expose it to view. The right adrenal so exposed was very much hypertrophied, probably 3 times the size of a normal gland. No adenomas were visible, the surface was regular and smooth. The wound was closed in layers and a similar incision made on the left side so that the left adrenal might be exposed. This was even slightly larger than the right, had a smooth surface, showed no adenomatous growth and was, therefore, resected after the blood-vessels entering it were ligated. A cigarette drain was placed in the vault, the kidney was repositioned and the wound was also sutured in layers. The drain was removed in 48 hours and the wound treated like that of a nephrectomy or pyelotomy operation. Primary union was obtained on the eighth day, the sutures were then removed and the patient proceeded to convalesce uninterruptedly.

The measurements of the gland were as follows:

Length	62 mm
Width	39 mm
Thickness	11 mm
Weight	16 grams

The gland is embedded in soft yellow fat tissue. It takes careful preparation to separate this from the surface of the gland. The gland itself is light

yellow in color and fairly soft to touch. Its substance is somewhat friable, as a result of which the gland was slightly injured on removal. Sections made perpendicularly to the longest diameter of the gland show a rather broad cortex which divides clearly into 2 strata. The outer layer which is about 3 mm in width is of bright yellow color. The other stratum is of a darker brownish color. Compared to the bulk of the cortical tissue there is but scanty medullary tissue present. Only at the lower pole and corresponding to the hilum of the gland are more substantial amounts of medullary tissue found.

*Microscopical examination* shows that the glomerular layer of the cortex has practically disappeared inasmuch as the fasciculata reached up to the capsule. The cells of this layer are very large and look like plant cells. The vacuolar character of these cells ceases almost abruptly, for the polyhedral cells of the deeper stratum are well stained and their cytoplasm is finely granular. These cells stain quite well with eosin but they are slightly basophilic. The solid mass of these cortical cells shows scattered islands of vacuolar cells similar to those of the outer stratum. The central portion of the cortical tissue surrounding the larger vessels or bordering on the medullary tissue shows a great deal of brown, finely granular pigment.

The cells of the medullary tissue are large, polyhedral, with abundant chromaffine granulation. They are imbedded in a fine reticulum and separated by a multitude of capillaries, most of which seem to be collapsed. The larger veins of the gland, particularly those close to the hilum, show well developed musculature.

#### RESULTS OF TREATMENT.—

The convalescence was uneventful, the

patient leaving the hospital with both wounds healed 14 days after operation. During her stay the highest temperature was 100° F (37.8° C) on the second day postoperative. The blood-pressure, which 2 days after operation was 105/62, rose so that on the sixth day it was 146/68. On discharge it was 110/60.

The first month she lost 25 pounds and thereafter 15 pounds a month, so that on October 8, 1930, she weighed 190 pounds, having lost a total of 145 pounds. This loss is even more significant because before she came under observation she had received 12 grains (0.77 Gm) of thyroid extract daily over a period of 9 months, with a total loss of weight of only 17 pounds, following which period she gained 125 pounds in the course of a year. At the time she took thyroid treatment her basal metabolic rate had risen to plus 38 per cent. For the first 2 months after her operation she menstruated every 2 weeks and since then her menstrual periods have been regular every month for a period of 5 days.

Six weeks after operation the patient reported the observation that the hair on her head had lost its normal curl and become quite straight.

Her nocturia has been reduced to twice a night. Her appetite is normal. It is to be stressed that since operation, she has received no medication, nor has she been subjected to any dietary restrictions.

The striking results obtained in this case by **unilateral adrenalectomy** vividly demonstrate the value of reducing the mass of hyperactive cortex in the treatment of this type of obesity. The rationale is similar to that of subtotal thyroidectomy for hyperthyroidism.

The success of this operation induced the authors to try the same in another

case which they believed might have a similar pathological basis, in spite of certain clinical differences, such as fat forearms and legs, broad, heavier bones in the hands and feet, heavy bones in the face with marked molar prominences, normal menstrual history. Surgical exploration, however, revealed adrenals of not more than ordinary size. Histological examination of one of the glands, removed at operation, failed to demonstrate changes of the cortex. The postoperative observation of this patient did not show any noteworthy depletion of the fat deposits.

This observation emphasized the importance of an accurate diagnosis of adrenal cortical hyperfunction before the removal of an adrenal for the cure of obesity, nor should an adrenal gland be removed before the other gland has been inspected. This is particularly important in the cases where the adrenal lesion consists of a unilateral adenoma, in which the other gland might appear practically normal. In a case of bilateral hyperplasia like the one reported here, the choice remains with the surgeon who probably will find it easier to remove the left gland.

**ONCHOCERCOSIS.**—The eye symptoms in onchocercosis have been found by Rafael Silva (Am J Ophth 14 518 (June) 1931) to be due to the microfilariae which penetrate the eye. He also found that sand flies were responsible for the disease and advises the adoption of means to prevent their breeding and their access to workmen. The best therapeutic results are yielded by **extirpation of the cysts.**

**OPHTHALMIA.—OPHTHALMIA NEONATORUM.**—*Etiology.*—A distinct type of ophthalmia neon-

atorum due to organisms other than gonococci can be demonstrated on proper bacteriologic investigation, according to N K Lazar (Arch Ophth 6 32 (July) 1931). Epithelial scrapings rather than the smear should be used for this purpose. In a series of 80 cases of ophthalmia of the newborn, 36 were of gonorrheal origin.

### **OPTIC CHIASM.—TUMORS.—**

*Treatment.*—G J Heuer (Surg Gynec Obst 53 489 (Oct) 1931) has traced the development of the surgical approach to the pituitary region, showing its gradual development into the present methods utilized to expose this difficult portion of the brain. Heuer's own method offers many advantages over those elaborated earlier and certain methods still in use. The Krause-Frazier method of transfrontal craniotomy is widely used. Frazier's recent modifications offer the advantage of a minimum of scar, because the scalp flap is so distant, so as to be reflected anteriorly over the eyebrow, whereas the bone flap follows the mid-sagittal plane and the orbital ridge to be reflected laterally and posteriorly hinging on the temporal muscle. This permits elevation of the frontal lobe with the head hanging over the edge of the operating table. A satisfactory view of the pituitary fossa is obtained, the dural opening being along the floor of the orbit and wing of the sphenoid. Heuer's approach is a lateral frontal exposure, approximately covering the area of the temporal muscle, with approach to the pituitary region along the wing of the sphenoid. This undoubtedly offers more room for displacement of the frontal lobe as well as retraction of the temporal lobe, but may be associated with some technical difficulties arising from the venous

emissaries along the greater wing of the sphenoid

The transsphenoidal method and its modifications have been more or less limited to intrasellar growths where visual field disturbances are present. It is the consensus of opinion that the transfrontal intracranial approach is more satisfactory and offers a better opportunity to deal directly with lesions arising in the pituitary region.

Heuer points out the 10 tumors which occur most frequently in this area.

1 The *chromophale adenomata* associated with acromegaly, where operative treatment is advocated when visual field disturbances occur. In 2 cases of Cushing's there was recession of the acromegaly following partial removal of the enlarged gland. X-ray treatment has assisted in the headache and in retarding the growth of the gland. Treatment is advised provided progressive visual field disturbances are not present. When danger to sight is evident, the tumor requires surgical intervention.

2 The *chromophobe adenomata* associated with, or without, Froehlich's disease. The disturbance of sex function, adiposity, as well as disturbances in the basal metabolic rate are not influenced by surgical removal of these tumors. X-ray treatment is of some value and should visual field disturbances occur, removal of the tumor is justifiable by surgical method.

3 *Suprasellar Adenomata*—The appearance of these lesions occurs frequently above the pituitary and without the signs of intrasellar involvement, the visual disturbances being primarily characterized frequently by a lack of general pituitary symptoms—a point of differential diagnosis which is of value in separating these from intrasellar lesions.

4 *Pituitary adenocarcinomata* require operative removal, the results of which are not recorded.

5 *Intrasellar Cysts*—These present surgical problems of drainage with attempts at partial removal when pressure on the optic nerves and chiasm warrants the intracranial approach.

6 *Suprasellar cysts*, Rathke's pouch type. These compress the chiasm from above. They frequently show deposits of calcium in their walls and vary in size from a small pea to a lemon. They are slow in growth and frequently produce a gradual visual field loss with failure of vision associated with mental hebetude and optic atrophy. The operative approach is the transfrontal route and it is the consensus of opinion that complete removal of this type of cyst is almost impossible as it is associated with an extremely high mortality. On the other hand, the conservative procedure of opening the cyst wall with frequent drainage with each recurrence seems to offer better possibilities.

7 *Suprasellar meningiomata* are slow growing benign tumors assuming, as a rule, a spherical shape and presenting a granular mulberry-like surface. They arise from the meninges over the tuberculum sellae. X-ray treatment has been found to be of no avail. Fifteen cases are reported by Cushing, 12 survived operation and the tumor was apparently totally removed in 8, incomplete in 4, and 6 of the 8 showed improvement in vision. Of the 4 partial removals, 1 showed slight improvement and 3 failed to improve.

8 *Parasellar meningiomata* (olfactory groove, sphenoidal ridge, meningiomata), these often reach astounding size before symptoms develop. The classical characteristic symptoms are anosmia, homolateral optic atrophy, a

contralateral choked disc and mental deterioration (Foster Kennedy's syndrome). Operative removal is difficult and is associated with a high mortality, although **partial removal with the electric cautery** and 2- or 3-stage operative attempts have been recorded. Cushing reports the successful **removal** of 4 of these large tumors.

9 *Ghomata of the optic nerves and chiasm*, are difficult to definitely diagnose. This condition gives rise to headache, visual disturbances, optic atrophy and field defects, with a flattening of the sellæ and clinical evidence of hypophyseal deficiency. In 33 per cent of his series, von Recklinghausen's disease was associated with this type of glioma. The period of survival reported is from 4 to 7 years.

10 *Ghomata About the Infundibulum*—As these tumors present the problem of a third ventricle lesion, removal is impossible and rapid recurrence usually takes place, the increase of intracranial pressure and the vagueness of symptoms frequently confuse them with cerebellar tumors.

Heuer points out the importance of *chronic cysternal arachnoiditis* which may be confused with a tumor. This produces primary optic atrophy and visual field defects. The sella is normal and the field defects are those of concentric contraction. The author reports visual improvement in 3 to 4 cases in which this condition was encountered at operation.

J. W. Kernohan, H. W. Woltman and A. Adson (Arch Neurol. and Psychiat 25:679 (Apr) 1931) present studies on 51 *extramedullary tumors of the spinal cord* verified at operation and 40 others in which decompression was effected, but tissue verification was not possible. The average duration of

symptoms extended over  $4\frac{1}{2}$  years and usually exceeded the time elapsing in extramedullary tumors, although this differentiation was not always possible before operation.

The sensory disturbances of intramedullary tumors gave a variability, with more marked involvement, covering several segments at the level of the lesion, and profound disturbances in the segments below the level of the tumor. Extramedullary tumors, on the other hand, frequently produce sharp levels of sensory demarcation with compression signs that uniformly involve the segments below the level of the tumor. **Operative intervention** consisted of an exploration, with splitting of the cord substance to permit extrusion of the tumor, complete removal of the tumor in a few cases, and **decompression of the cord** alone was undertaken in 40 cases.

**OPTIC NERVE.—ATROPHY.**  
—*Classification.*—L. Paton (Proc Roy Soc Med (Sect Neurol) 24:15 (Nov) 1930) classifies optic atrophies according to the site of attack of the primary lesions and subdivides them according to the nature of the lesion. He subdivides the optic nerve into (a) the retinal portion, (b) the papillary portion, (c) the retrobulbar portion.

(a) In atrophy due to retinal degeneration, the disk is waxy and its outline clearly defined. The vessels are characteristically diminished in caliber. This type of atrophy occurs in primary atrophy associated with retinitis pigmentosa, amaurotic family idiocy, cerebromacular degeneration and secondary atrophy of the retina following chorio-retinitis and vascular degenerations.

(b) In the papillary atrophies the initial damage to the nerve fibers takes



place at the disk itself. This type occurs in glaucoma, papillitis, papilledema, traumatic avulsion of the optic nerve, and in cavernous degeneration in the disk of high myopes.

(c) Atrophies due to retrobulbar lesions, orbital, foraminal or intracranial, form the largest group. Disseminated sclerosis, postinfluenzal myelitis, syphilitic myelitis, Malta and black-water fever, postherpetic neuritis, and postvaricellar neuritis belong to this type. The retrobulbar portion is subdivided into (1) the orbital, (2) the foraminal, and (3) the intracranial. Tumors acting on the orbital portion of the optic nerve may cause optic atrophy. Trauma is the most frequent cause of foraminal lesions giving rise to optic atrophy. Pressure atrophy caused by growths is the main intracranial form of atrophy. Optic atrophy may also be caused by tobacco, arsenic, lead, methyl alcohol, carbon bisulphide, quinine, aspidium filix mas, and systemic degenerations in the central nervous system, such as Friedreich's disease, peroneal atrophy and hereditary cerebellar atrophy. Two types of optic atrophy occur in tabes. In one, the parenchymatous degeneration predominates, in the other, the interstitial proliferation is more evident.

**Etiology.**—A case of bilateral optic atrophy is reported by G. H. Hogg (Med J Australia 2.160 (Aug 3) 1929) in a 3 year-old child suffering from *whooping cough*. He has collected 7 other cases of optic neuritis in whooping cough. In 5 of these recovery took place and in 2 atrophy followed.

The case is reported by F. Terrien (Presse méd 38.953 (July 16) 1930) of a woman, aged 58 years, who, 9 days after severe *hematemesis*, woke up completely blind. Both disks showed

primary atrophy. Visual disturbances have been reported following *hematemesis*, *metrorrhagia* or trauma. Blindness usually comes on after repeated bleeding, rather than after a single severe hemorrhage. The *prognosis* is unfavorable. Subcutaneous injections of **acetylcholin** reduce the general blood-pressure through elective dilatation of the arterioles, and have been known to double the caliber of the central artery of the retina and to improve the visual field greatly. They were, however, of no benefit in Terrien's case but were not used until optic atrophy had been present for 3 months.

**Pathology.**—*Hereditary optic atrophy* or *Leber's disease*, is rare, but bears a distinct relationship to other heredodegenerative conditions of the central nervous system, according to H. H. Merritt (Arch Neurol and Psychiat 24 775 (Oct) 1930). A case is reported of a man who began losing vision at the age of 26. The previous history was comparatively insignificant, the only noteworthy condition being frontal headaches for some years. There was a family history of a maternal uncle having the same trouble at 30, another uncle had trouble with his eyes some years prior to his death at 34, and a maternal second cousin had the same trouble. High arched feet similar to a Friedreich's foot was present in the mother and patient, and webbing of the toes in the patient and his father. Neurological examination was negative except for the optic atrophy.

The characteristics of the eye condition are that it progresses rapidly for a few weeks and then remains stationary, rarely, if ever, progressing to complete blindness. Improvement may occur. Merritt states that the visual loss is practically always a central (rarely

paracentral; scotoma for white and colors or for colors alone, with normal peripheral fields. In the early stages the fundus picture is that of an axial neuritis, later, it is one of postneuritic optic atrophy involving chiefly the temporal fibers.

The *diagnosis* depends largely on a history of familial eye defect coming on, like other abiotrophies, comparatively early in life and the typical optic atrophy.

K Rehsteiner (Schweiz med Wchnschr 60 122 (Feb 8) 1930) reports a case of *hereditary optic atrophy* (*Leber's disease*) in a young man who up to the age of 39 had normal vision. When vision failed, examination revealed a central scotoma of both eyes, which gradually increased in size. The peripheral field was not impaired. When the patient died several years later, due to encephalorrhagia, microscopic examination showed primary atrophy of the nervous elements, with proliferation of the neuroglia in the optic nerve, and atrophy of the ganglion cells in the central part of the retina which by their location indicated involvement of the papillomacular bundle. Leber's disease is hereditary and is more frequent in men than in women. Vision is normal until the second or third decade.

**Treatment.**—Twelve cases of tabetic optic atrophy were treated by J. Fried (J. Nerv. and Ment Dis 73 487 (May) 1931) with a sulphur and bismuth compound. The diagnosis in 11 cases was locomotor ataxia, and taboparesis in 1 case. One cc (16 minims) of bismuth salicylate was given intramuscularly. This was subsequently increased to 1.5 cc (24 minims), and associated with Winkler's bismuth and sulphur salicylate compound. The

visual acuity was at first impaired but was followed by marked improvement which persisted. Color vision returned to normal, and the visual fields showed progressive improvement.

**NEUROMYELITIS.**—A peculiar form of optic neuromyelitis, which presented some characteristics of encephalitis periaxialis was observed by G Marinesco, S Draganesco, O Sage and D Grigoresco (Rev neurol 2 193 (Aug) 1930). They are of the opinion that, although optic neuromyelitis and Schilder's disease are 2 separate infections, this type of case demonstrates that a certain relationship exists between them. In the case reported lesions in the medulla were indicative of optic neuromyelitis, while lesions in the cerebrum were suggestive of Schilder's encephalitis periaxialis.

**RETROBULBAR NEURITIS.**—**Etiology.**—It is believed by S R Gifford (Arch Ophth 5 276 (Feb) 1931) that more than 50 per cent of cases of retrobulbar neuritis are caused by multiple sclerosis, 35 per cent are due to purulent sinusitis. He is of the opinion that latent or hyperplastic sinusitis may cause retrobulbar neuritis, but he stresses the importance of eliminating multiple sclerosis and brain tumor and advises careful examination of the spinal fluid with reference to the gold curve and cell count. In some cases exploratory operation of the sinuses is indicated.

E S. Thomson (Arch Otolaryng 10.248 (Sept) 1929) considers that sinus disease is responsible for a considerable proportion of the cases of retrobulbar neuritis, plastic neuritis, and a form characterized by sudden functional depression with no change in the appearance of the optic nerve. The neuritis is the result of direct infection

from the ethmoids and sphenoids and is not toxic. Good results usually follow early operation on the sinuses.

**Diagnosis.**—In order to diagnose chronic retrobulbar neuritis W. H. Wilmer (Arch. Ophth. 4: 817 (Dec.) 1930) stresses the importance of the following, *ie*, detailed family history, examination of blood, spinal fluid, visual fields and sinuses, and a search for evidence of pituitary body disease. In differential diagnosis, sex, family history, and the absolute central scotoma in Leber's disease are of value.

**Treatment** should be directed toward removal of foci of infection and the treatment of toxemias, *eg*, syphilis, tuberculosis, or diabetes. In chronic cases exploration of the sinuses is advisable.

**ORBIT.—CELLULITIS.—Etiology.**—The 3 chief causes of orbital cellulitis in order of frequency, according to E. T. Smith (Brit. M. J. 2: 14 (July 5) 1930), are: (1) nasal sinus infection, in which not only proptosis but a characteristic outward displacement occurs. The ethmoids or antrums should be explored. The result is usually good, (2) skin infections, *eg*, impetigo, fly-bites, boils, etc. In this type, high temperature, cavernous sinus thrombosis, pneumonia, and death are likely to supervene, (3) osteomyelitis or periostitis of the orbit from a blood stream infection. This form is also very dangerous.

**Diagnosis.**—J. A. Babbitt (Ann. Otol., Rhin. and Laryng. 39: 444 (June) 1930) points out that the symptoms of acute orbital cellulitis and cavernous sinus thrombosis are very much alike. In both conditions the following conditions are found: exophthalmos, extension to the other eye, ptosis, rigid posi-

tion of the eyeball, pain, loss of vision, and toxemia. Four cases of orbital cellulitis are described in which cavernous sinus thrombosis was suspected but not proved. Babbitt believes that orbital cellulitis, which he considers a symptom-complex rather than an entity, arises from nasal disease except in cases of obvious external cause. The importance of initial sinus surgery in doubtful cases is emphasized.

**Treatment.**—In 1 of the 3 cases of orbital cellulitis in children seen by E. T. Smith (*loc. cit.*), the eye was saved by early incision and drainage. In the other 2, incision was delayed, the condition extended, and sloughing of the cornea followed as a result of interference with its nutrition. Smith emphasizes the importance of early drainage of the orbit, if relief is not obtained by sinus operation, in order to save the eye from corneal sloughing, which may result from exposure and interference with its nutrition.

In discussing the management of orbital infections, John Green (Am. J. Ophth. 14: 196 (Mar.) 1931) considers that conservative methods are adequate in some cases, while moderate and sometimes radical surgical intervention is necessary in others to control the inflammation and to save the lives of the patients.

**TRAUMA.**—Two cases of trauma in which the eyeball was surrounded by a transparent ring, visible by x-ray, are reported by D. Perotti (Rassegna internaz. di clin. e terap. 11: 623 (Sept.) 1930). It was thought that air entered the orbit from the ethmoid sinus through the fractured lamina papyracea and caused emphysema of the fatty tissue of the orbit rather than of Tenon's capsule. The infiltration of air disappeared and caused no trouble.

**XANTHOMATOSIS.**—A case of xanthomatosis in a 4-year-old child, reported by E B Dunphy (New England Ophthalmological Soc (Jan 20) 1931, Am J Ophth 14 1048 (Oct) 1931), presented the following symptoms: thirst, frequent micturition, loss of weight, proptosis of the left eye, a prominence in the occipital region and defective speech. An operation on the orbit to remove the yellow tumor tissue was unsuccessful and enucleation was performed.

**OSTEOMYELITIS.**—*Carcinoma* is a rare complication of long standing osteomyelitis, according to E B Benedict (Surg Gynec Obst 53 1 (July) 1931), occurring more often in the tibia than any other bone. While growth is easily diagnosed when superficial, this is very difficult when it is deep-seated. X-ray may often show typical moth-eaten appearance of carcinoma. The treatment is early **amputation**. The prognosis is usually favorable, the condition being of low malignancy.

**TREATMENT.**—A very delightful and thorough study of the treatment of chronic osteomyelitis with the maggot (larva of the blow fly) is presented by W S Baer (J Bone and Joint Surg 13 438 (July) 1931). He briefly reviews the history of the **maggot treatment**, the life history of the blue and the green bottle fly, the technic of raising maggots, their therapeutic use, and the results of cases treated by this method. This writer believes that the maggot has been found to be a useful adjunct to a thorough surgical treatment of chronic osteomyelitis and that they are far more successful in securing permanent healing than any other method used by him. Maggots, by their diges-

tive action, clear away minute fragments of bone, cause wounds to become alkaline, and in this way diminish the growth of bacteria.

**OVARIAN ORGANOTHERAPY.** See ANIMAL EXTRACTS

**OXALURIA.**—In the routine examination of numerous specimens of urine it is not uncommon to find the octahedral crystals of calcium oxalate. Apart from the fact that calculus formation may arise therefrom, their presence is not given much significance by clinicians. In many instances, patients pass large quantities of individual calcium oxalate crystals with no inconvenience. According to J V C Braithwaite (Brit M J 1 15 (Jan 4) 1930), this absence of urinary symptoms is all the more remarkable when the effects of oxalic acid and soluble oxalate upon the kidneys are considered. Many workers have reported that the introduction of these substances results in an acute tubular nephritis. Braithwaite quotes Shaw-Dunn and his co-workers as saying that the deposition of calcium oxalate in the tubules plays no important part in this process.

During the years 1926 to 1930, 4 persons were admitted to the Royal Infirmary at Leicester who were suffering from oxalic acid poisoning. In only one fatal case was there suppression of urine.

Three anonymous correspondents in the Lancet reported symptoms in themselves as a result of the ingestion of rhubarb, attributing their condition to the oxalic acid in the edible. Of these, 1 had dysuria and blood in the urine, 1 had dysuria alone, and 1 had no urinary symptoms.

According to Braithwaite, there is much evidence to believe that oxalates

in a state of solution are highly toxic to the kidney and it would appear that the absence of serious symptoms in individuals passing calcium oxalate is dependent on the extreme insolubility of the lime salt. Formerly it was thought that the sodium phosphate held the calcium oxalate crystals in solution for some time after the urine was voided. This is not the case, as shown by the frequency of the crystals seen in freshly passed acid urine.

Presumably, then, calcium oxalate is sometimes excreted as such by the kidney. The author believes that there is a mechanical element which must be taken into consideration in explaining the damaging effect of this salt upon the kidneys.

The author states that, of course, it would be useless and foolish to generalize upon the one case which he reported in the article but he does suggest that the passage of calcium oxalate crystals is not always as innocuous as supposed and that some cases of unexplained spontaneous hematuria may be due to a similar cause. Although calcium oxalate can cause some mechanical damage to the kidney the absence of symptoms, the rapid recovery, the normal blood-pressure, and particularly the normal blood urea of his particular patient, show that is the safest form in which the body can excrete any abnormal accumulation of oxalates in its substance.

**OXYGEN AND OXYGEN THERAPY.**—D Jahn (Klin Wchnschr 9 1757 (Sept 20) 1930), in commenting on the theory of Hill that increased oxygen consumption after bodily exercise is due to oxidation of the lactic acid that forms in the muscles, states that he believes this theory is obsolete because he has been unable to prove a

quantitative relation between lactic acid formation and oxygen consumption. He feels that the increased oxygen consumption is due to an irritative action caused by the lactic acid which has been formed. He has injected lactic acid intravenously and then measured oxygen consumption and finds that the oxygen used is out of all proportion to that which should be required to oxidize the given amount of lactic acid. He states that the irritative action probably involves a number of factors and is dependent on the condition of the sympathetic nervous system.

A L Barach (Ann Int Med 5 428 (Oct) 1931) studied the use of oxygen in patients suffering from various types of heart failure. He noted, in those cases with **congestive heart failure**, a marked relief of dyspnea and orthopnea, diuresis and disappearance of edema, with a marked rise in the carbon dioxide content of the arterial blood following oxygen administration. Other observers also notice relief from cyanosis and a lowered pulse rate with a decrease in the lactic acid content of the blood. In those cases of **acute coronary thrombosis** some benefit seemed to be derived with prolongation of life when inhalation of oxygen-enriched atmosphere was given. In many cases, life was prolonged sufficiently for the heart to be able to recover from its acute functional disturbance and carry on its usual work. Barach feels that the clinical improvement seen in the various types of heart failure following the use of oxygen therapy warrants its admission to the field of therapeutic agents used in this disease.

Commenting on the value of oxygen therapy, R. L. Cecil and N. Plummer (J A M A 95 1263 (Oct 25) 1930) suggest a simplified apparatus for oxy-

gen administration This apparatus is based upon the use of tanks of oxygen with an oxygen tent, a cooled air system which is cooled perfectly by dry ice, and a system of valves adjusted in such a manner that the pressure of the oxygen, in coming from the tank to the tent,

causes aeration of the tent and change of air, thus relieving the necessity of a motor-driven apparatus The entire unit is easily movable from place to place and, therefore, supposedly has an advantage over the various oxygen chambers, etc

## P

**PAGET'S DISEASE AND OSTEOGENIC SARCOMA.**—It is recalled by B L Coley and G S Sharp (Arch Surg 23 918 (Dec ) 1931) that Sir James Paget mentioned the tendency in patients with osteitis deformans to develop malignant growths in his earliest communication concerning the disease in 1877.

Both Paget's disease and osteogenic sarcoma are such relatively rare diseases that the occurrence of the latter in as high as 95 per cent of the former, as related by J C Da Costa and others, cannot be mere coincidence

**PROGNOSIS.**—The average duration of life after sarcoma is first detected in a case of osteitis deformans or Paget's disease is about 15 months, varying from 2½ months to 2 years Paget's disease may precede the advent of sarcoma by as much as 20 or more years, but with the appearance of the sarcoma, the disease is always fatal

The complicating sarcoma occurs after the age of 55 years, and is most frequent at 65 to 70 years Paget's disease usually occurs after the age of 35, and usually precedes the complicating sarcoma 10 or 15 years

**TREATMENT.**—There is no satisfactory treatment for Paget's disease complicated by osteogenic sarcoma Various methods, such as x-ray, radium, and mixed bacterial vaccines, have been

tried without success, and no case has been known to live 5 years

**PAGET'S DISEASE OF THE NIPPLE.** See CANCER

**PANCREAS, DISEASES OF.**—

**—X-RAY DIAGNOSIS.**—Regarding the clinical diagnosis of pancreatic disease, J T Case states that the present status leaves much to be desired (Trans Am Gastro Enterol A 31 138, 1929) In this organ, as in the liver, the immense reserve makes functional tests of little value in any but well advanced cases According to this author, the 2 most important clinical syndromes which should attract attention to the pancreas are solar plexus pain and obstructive jaundice, otherwise the symptoms of pancreatic disease are vague X-ray can only aid in diagnosis when alteration of size or contour is present, when alterations of duodenal motility occur, or when calculi are present Direct methods of x-ray examination were not successful until artificial pneumoperitoneum was developed This procedure is associated with some risk and considerable annoyance and is probably not justifiable except in rare cases of pancreatic cyst An exploratory operation, the author believes, is only slightly more risky and is far more informing



*Pancreatic stones* are usually small, seldom being larger than a walnut, according to Case. They are usually multiple, occasionally filling many ducts. They usually consist of calcium carbonate or phosphate. On the x-ray film they usually appear as round or irregular shadows lying in the neighborhood of the first and second, sometimes the upper border of the third, lumbar vertebrae. They are usually nearer the midline than either gall-stones or nephroliths. Cholecystography and pyelography may be necessary in some cases for differential diagnosis. Calcified mesenteric glands are usually scattered over a wider area and may be movable. Calcification of an artery or the aorta may be confusing in some instances, but lateral plates will aid in the differentiation.

Case (*loc cit*) states that of all the lesions of the pancreas, those which alter its normal contour, such as cysts and tumors, are best adapted for x-ray demonstration. According to their origin, pancreatic *cysts*, when of sufficient size, may displace the stomach and colon downward; the stomach upward and the colon downward, the stomach and small intestine downward with compression of the colon, or the stomach and colon upward while compressing or displacing downward the small intestine. *Tumors* of the head of the pancreas may widen the arch of the duodenum, or cause a filling defect of the pyloric end of the stomach, while tumors of the tail are more likely to distort the outline of the greater curvature of the stomach and left half of the colon. Further aids to x-ray diagnosis, according to the writer, are the use of air injection into the stomach, an opaque meal, and palpation under the fluoroscope.

*Carcinoma* of the pancreas may give rise to a number of different manifestations susceptible of x-ray demonstration, states Case (*loc cit*). A filling defect may be seen on the greater curvature of the stomach, or possibly a "pad defect" in the middle of the body of the stomach. Gastric displacement or an hour-glass may be seen. Palpation under the fluoroscope is necessary in such cases to rule out intrinsic gastric lesions. Duodenal changes are frequent findings in malignancy of the head of the pancreas. Altered motility and widening of the duodenal curve are the most common findings. In some cases there is great irregularity, making possible a differentiation between carcinoma and cyst. Constriction and duodenal stasis may occur. Niche-like projections occasionally occur simulating diverticula or ulcer. The latter has never been seen below the first portion of the duodenum by the author, and the outline of a benign diverticulum is usually smooth.

*Chronic pancreatitis* usually gives evidence by x-ray only when enlargement has occurred. Case states, however, that in several instances in which a duodenal diverticulum had been seen on the inner side of the second portion of the duodenum, chronic pancreatitis with dilatation of the ampulla of Vater was found at operation or autopsy. Several cases of acute pancreatic symptoms have been found due to duodenal diverticulum extending into the pancreatic tissue with acute inflammatory changes occurring. Gastric or duodenal ulcers occasionally invade the pancreas. Such a condition may be suspected when the ulcer niche fails to move with respiration, according to this authority.

**ACUTE PANCREATITIS.**—Because of the apparent increasing frequency of acute pancreatitis, and be-

cause of the staggering mortality of 50 per cent, the unsolved riddle of the etiology, the high index of incorrect diagnosis, and the lack of unanimity of opinions as to the proper treatment, E L Elhason and J P North (Suig Gynec Obst 51 183 (Aug) 1930) believe the subject needs increased consideration

**Etiology.**—As to etiology, the authors state that in their series of 13 cases, associated biliary disease was present in 71 per cent. A history of attacks of *dyspepsia* suggesting gall-bladder pathology preceding the acute attack of pancreatitis is said to be customarily found in these patients. In 96 histories, 62 noted epigastric or right hypochondriac pain of at least a year's duration. This sequence of chronic cholecystitis and acute pancreatitis is too common and too important to be ignored, the authors state

From the experimental standpoint, 2 problems are met: the nature of the substance producing premature intraglandular activation of trypsinogen, and the mode of access of this substance to the pancreas. Various substances have been used, *i e*, bile, duodenal contents, chemical irritants and bacterial cultures. The authors state that the only safe conclusions which can be drawn are that the introduction into the pancreatic duct of almost any irritating foreign substance, together with damage to pancreatic cells, either traumatic or otherwise, will produce activation of enzymes and consequent tissue autolysis

The pancreatic duct and the lymphatics offer 2 means of access to the pancreas; the blood stream and direct extension are regarded as problematical sources, according to these writers. Opie, in 1903, proposed the theory that obstruction of the common duct at the

ampulla of Vater with regurgitation of bile into the pancreas might cause the disease. It was found by Mann and Giordano that the anatomical formation necessary to this theory only occurred in about 35 per cent of persons. They also found that the pressure necessary to produce pancreatic lesions was in excess of any obtained under physiologic conditions. Other authors including Deaver, Pfeiffer and Sweet believe in the lymphatic theory, basing their contentions upon (1) the frequent coincidence of biliary disease, particularly cholelithiasis, (2) clinical cures following cholecystectomy and common duct drainage without direct attack upon the pancreas, and (3) obvious defects in the regurgitation theory. The work of Graham demonstrated lymphatic connections between the gall-bladder, duodenum and pancreas by dye injection

**Symptoms** are variable and may simulate acute cholecystitis, acute intestinal obstruction, perforated ulcer, and acute appendicitis, according to Elhason and North (*loc cit*). In case reports studied by them a correct diagnosis was made in only 31 per cent. The onset of pain may follow food, but this relation is not of diagnostic aid, since frequently the attack has no food relation. In 27 per cent of the cases collected, the pain was referred through to the back, to one or both shoulders in 7 per cent, and to the left upper abdomen in 6 per cent. The pain is usually very severe. Ogilvie is quoted as saying that "in acute perforated ulcer, the patient never moves from the place when the pain has felled him, in acute pancreatitis, however, he may go to work after the onset." The authors have observed that the patients with acute pancreatitis tend to form a right lateral decubitus position in bed. Vomiting is

usually persistent. A slate-grey cyanotic appearance of the upper portions of the body has been described which, when present, is said to be pathognomonic. In 200 reported cases it was observed in 40 per cent. Tenderness is a constant finding, but may vary in location, the authors state. Rigidity is seldom marked. Leukocytosis is usually marked. Urinary diastase is said to be increased, although the authors have had no experience with that test. Loewi's adrenalin test was not of value in this series.

**Prognosis**—The following figures regarding prognosis were compiled by the authors from the literature.

Pathology	Cases	Mortality, Per Cent
1 None except for fat necrosis	4	25
2 Pancreatic edema and fat necrosis	42	24
3 Pancreatic hemorrhage, or necrosis, or both	61	65
4 Gangrene	7	71
5 Abscess	6	33

**Treatment**.—Immediate operation is the accepted treatment in this country, according to Eliason and North (*loc cit*), but their own experience lends some doubt as to the rationality of this plan. Of 8 cases operated upon within 48 hours, 6 died, on the other hand, 5 patients, upon whom operation was deferred for from 4 to 9 days, all recovered. *Complications to surgery* in this disease include intractable bleeding, pancreatic asthenia, defective wound healing, residual abscess, and recurrences.

**ACUTE HEMORRHAGIC PANCREATITIS**—J. W. G. Grant (Brit M J 2 1084 (Dec 12) 1931) agrees with Opie and Archibald, as do most surgeons of today, that the usual cause of acute hemorrhagic pancreatitis is the

flow of bile into the pancreas due to blocking of the common bile duct, usually by a small gall-stone, the point of lodgment of the stone being the ampulla of Vater.

At operation, there is blood stained peritoneal fluid, and more or less extensive fat necrosis of the omentum. The pancreas is swollen and red, resembling raw beefsteak. The gall-stones are usually minute cholesterol stones.

**Operation** consists of suturing a drainage tube into the gall-bladder and carrying a drain through the omentum to the pancreas.

**PANCREATIC FUNCTION TESTS**.—The chemical tests of pancreatic efficiency have been summarized by G. A. Harrison (Lancet 1:1249, 1305 (June 7, 14) 1930), who points out that here, as in the case of the kidneys, the tests yield abnormal results only when extensive disease is present. The pancreas has a large reserve, and nonpancreatic factors, such as biliary disease, must be considered. In general, the functions of the pancreas include the formation of the internal secretion (insulin) and the formation of the external secretion containing the enzymes amylase, trypsin, and lipase. The author states that in diseases of the pancreas as a whole, and especially in chronic disease, *hyperglycemia* and *glycosuria* are rarely found except in advanced conditions involving a large proportion of the islands of Langerhans.

**Loewi's test** consists of observations of the pupils before and after instillation of 2 drops of 1:1000 adrenalin into one eye. The treated eye normally shows no change when observed every 15 minutes for an hour. A positive test is present if dilatation occurs, eccentric dilatation is not uncommon. The test is explained by assuming that the

autonomic nervous system is hypersensitive, due either to hypoinsulinism, or to irritation of the solar plexus. Positive tests may be obtained in hyperthyroidism, and in biliary disease. Negative results may be obtained in typical cases of acute pancreatitis, the author states.

Tests of external pancreatic secretion are discussed by the writer under the heading of each enzyme as follows

**Carbohydrate-splitting Ferment.**

—Gastric and duodenal examinations for this enzyme are useless, due to the presence of salivary ptyalin. Fecal examination is also usually unsatisfactory, due to bacterial action. According to Harrison (*loc cit*), the most satisfactory test is that of diastase in the urine by the method of Wohlgemuth. By this method a unit is the amount of diastase which will digest 1 cc of 0.1 per cent soluble starch in 30 minutes at 37 to 38° C to such a degree that no blue color is obtained by adding iodine. The diastatic index is the number of units per cc of urine. In the normal the index is 6.7 to 33.3 units, or 8000 to 30,000 units output per day. An index of 50 is suspicious and of 100 almost always abnormal, according to the writer. In chronic pancreatitis and carcinoma of the pancreas the index is usually normal or low. Severe trauma may increase the index. It is usually normal in diabetes. In acute pancreatitis the results are usually over 100 but lesser readings are not significant.

**Protein-splitting Ferment.**—Examinations of the gastric and duodenal content for trypsin may be of some value. The presence of the enzyme excludes complete pancreatic obstruction, but absence is not conclusive. *Fecal examination*, in the author's opinion, is not of great value unless it is possible to

carry out complete nitrogen balance tests. In pancreatic disease fecal nitrogen is proportionally increased. The presence of muscle fibers presenting no signs of digestion, *ie*, retaining well marked striations and sharp ends, is significant of deficient trypsin, but their absence does not eliminate pancreatic disease, according to Harrison.

**Fat-splitting Ferment.**—Tests for lipase in duodenal fluid may be of use. If present, pancreatic obstruction cannot be present, but the absence of lipase does not indicate obstruction.

*Fecal examination* may present valuable evidence of pancreatic disease. Bulky stools are often seen in pancreatic dysfunction, but may also be seen in common duct obstruction, gastrocolic fistula, celiac disease, sprue, congenital steatorrhea, and mesenteric tuberculosis, according to the writer. True fatty stools, steatorrhea, is generally believed to indicate pancreatic disease. Microscopic examination to reveal the type of fat is often of help. When there is a deficiency of pancreatic juice, fat splitting is defective, the author states, hence the fatty excess is usually in the form of neutral fats. However, neutral fats may be hydrolyzed in the gut so that their absence cannot exclude pancreatic disease. In cases showing excess fat, chemical analysis may be undertaken. Normally, not more than one-quarter to one third of the dried feces is fat. In typical pancreatic cases, the author states, the total fat may reach 50 per cent, with 40 to 70 per cent being unsplit. The following table is given to show the results to be expected in normal and diseased persons using the simpler tests. (See next page.)

**Fecal Analysis in Chronic Pancreatic Disease.**—Although the value of fecal analysis in the diagnosis of

## PANCREATIC FUNCTION TESTS (HARRISON)

Condition	Loewi's Test	Glyco- suria	Hyper- glycemia	Urinary Dia- stase, Units per C c	Trypsin in Duode- nal Fluid	Creatin- in	Lipase in Duode- nal Fluid	Steator- rhea	Fat in Feces	
									Total Fat Per Cent in Dried Feces	Split Fat Per Cent of Fecal Fat
Health	0	0	0	67-333	+	0	+	0	Up to 25	75 or over
Acute pancreatitis	Often +	Often +	Often +	100-2000	—	0 or +	—	—	—	—
Pancreatic trauma.	0 or +	0 or +	0 or +	67-200	—	0 or +	—	Usually 0	Normal or raised	Normal or less than 75
Chronic pancreatitis	Usually 0	Usually 0	0 or +	Usually Normal	+ or ±	0 or +	+ or ±	0 to ++	Normal or raised	Normal or less than 75
New growth of pan- creas	Usually 0	Usually 0	Usually 0	67-100	+ or 0	0 or +	+ or 0	0 to ++	Normal or raised	Normal or less than 75
Chronic pancreatic duct obstruction	Usually 0	Usually 0	Usually 0	67-100	0	+	0	0 to ++	Usually 25-50 or more	Usually 75 30 or less
Diabetes mellitus	0	+	+	Normal or low	+	0	+	0	Normal	Normal
New growths of islets	0	0	Hypo- gly- cemia	Normal	+	0	+	0	Normal	Normal

pancreatic disease was pointed out by Friedreich, in 1875, the importance of this study is not yet common knowledge, according to Joseph Pratt (Internat Clin 3 164, 1931) He states that even today "there are surgeons who write papers on the diagnosis of cancer of the pancreas without even mentioning the character of the stools" Fat in the stools of patients with pancreatic disease may be in various forms, liquid or solid The type of fat probably depends upon the type fed, according to this writer, who has shown that in a dog with pancreatic obstruction the fecal fat is the same as that ingested In normal dogs, feeding of various fats does not change the type of fecal fat, which is said to be secreted by the intestinal mucosa

Fecal fat occurs as neutral fat, fatty acids and soaps Neutral fat usually occurs as droplets, which are often yellow, and may be single or may coalesce into larger masses Addition of an alcoholic solution of Sudan III colors the neutral fat red or orange Fatty acids appear as needle crystals, drops, or flakes Soaps form flakes or crystals Soap crystals are usually shorter, less pointed and less curved than fatty acid crystals On heating, neutral fat and fatty acid crystals are converted into oil drops but the soap crystals remain unchanged, the author states A simple method is suggested for determining roughly the amount of fat present A fecal suspension with a drop of 30 per cent acetic acid on a microscope slide covered with a cover-glass is heated If much fat is present nearly the entire specimen will be converted into fat drops

Bulkiness is an important feature of the stools in obstruction of the pancreatic ducts Pratt (*loc cit*) states

that in no other condition are such massive dejections seen This is the chief difference between pancreatic stools and those seen in uncomplicated obstructive jaundice "*The voluminous stool is probably the most important single subjective sign of pancreatic disease*" In a dog with pancreatic duct obstruction the author found that the weight of the fresh stools passed in a 4-days' test exceeded the weight of the animal

The use of a diet similar to that suggested by Adolf Schmidt is of value in pancreatic diagnosis The principle of such a diet is the administration of sufficient meat, fat and starch to put a test load on the pancreas The author quotes Schmidt as finding the following dried fecal weights in a 3-day test period in various conditions

	Grains
1 Normal, 6 cases, average	54.3
2 Obstructive jaundice, 4 cases	175.6
3 Hypochylia pancreatica, 2 cases	132.0
4 Obstruction of bile and pancreatic ducts, 1 case	419.0
5 Fermentative dyspepsia, 5 cases	127.4
6 Achylia gastrica with diarrhea	98.9
7 Severe enteritis	186.5

Pratt states that in distinguishing between biliary obstruction and pancreatic obstruction, the weight of the dried stool is usually a far safer guide than the percentage of fat present Another condition which must be borne in mind when fatty stools are present is sprue The author states that fecal analysis is of great aid in differentiating this condition from pernicious anemia, and from various types of diarrhea

Total nitrogen excretion in the feces is also of aid in the diagnosis of pancreatic disease Pratt, who has given the subject especial attention, believes that undigested muscle accounts for the higher figures in pancreatic obstruction The following figures are given



	Grams
1 Normal	0.99
2 Obstruction of common duct	2.05
3 Constipation	0.52
4 Diarrhea	1.57
5 Nervous diarrhea	1.07
6 Ulcerative colitis	1.72
7 Sprue	2.72
8 Sprue	1.59
9 Obstruction of common duct	1.11
10 Fatty diarrhea	2.15
11 Obstruction pancreatic ducts	8.49

*Starch digestion* in pancreatic disease has been little studied, according to this author. In jaundice, starch utilization appears to be equal to that in health. The greatest disturbance appears in catarrh of the small intestine. The writer investigated the effect of pancreatic duct occlusion in dogs. Starch content of the feces was determined by obtaining a clear fluid from a hydrolized suspension of feces and analyzing it by Folin's method. It was found in 2 dogs that pancreatic obstruction reduced starch absorption from 92 to 74 per cent and 95 to 64 per cent respectively. Careful feeding of these dogs resulted in fairly good absorption of fats, nitrogen and starch, in spite of the lack of pancreatic juice. Overfeeding, however, resulted in inanition and death.

### PAPILLEDEMA.—ETIOLOGY.

—Some interesting cases are reported by M. Balado and M. Ibanez Puiggari (*Semana méd* 1 1081 (Apr 23) 1931) in which edema of the disc was not due to brain tumor. In 1 patient who showed signs of intracranial hypertension, decreased vision, headache, vomiting, asynergy, ataxia, tremor, inability to stand, and negative spinal fluid, the x-ray, with the aid of lipiodol, showed small but normally shaped ventricles which excluded tumor. The small size of the ventricles was attributed to edema of the brain, which was probably caused

by a previous infectious disease. The cause was not found but the patient recovered after **decompressive trephine**.

The mechanical theory is accepted by G. W. Swift (*Arch Ophth* 3 47 (Jan) 1930), to explain choked disc. The general cerebral circulation depends on a free circulation within the transverse and sigmoid sinuses, while the orbital circulation depends on a free cavernous and petrosal circulation. They join partly at the sigmoid and totally in the jugular bulb. When one side is partially or temporarily blocked in a normal and symmetrical venous sinus system, compensation takes place but in asymmetrical embryonic malformations of the sinuses an imbalance of circulation is produced. In lesions of the cerebellar fossa choked disc denotes variations in the transverse, sigmoid and jugular bulb, because the constancy of the cavernous and petrosal sinuses is clearly established.

W. E. Fry (*Am J Ophth* 14 874 (Sept) 1931) studied 40 human optic nerves, cut in serial sections, with special reference to compression of the central vein of the retina. The cases included brain tumor, meningitis, brain abscess, gumma of the brain and aneurism. Thirty-two of the eyes presented papilledema. He found that compression of the central vein, either along the side of the nerve or in the subarachnoid space, produced a venous stasis with a consequent transudation of lymph into the tissues of the optic disc and adjacent nerve fiber layer of the retina, causing papilledema.

Forward pressure of fluid within the optic nerve by infiltration of cerebrospinal fluid under increased pressure he found to be a secondary cause. No inflammatory or toxic cause of papilledema was found.

**PARALYSIS AGITANS.** See  
BASAL GANGLIA

**PARATHYROID GLAND.—**

That *parathyroidism* is a condition frequently encountered if the symptoms are looked for and properly interpreted is attested by M Ballin and P F Morse (Am J Surg 12 403 (June) 1931) A general demineralization of the bones, with cystic areas and severe pains in the bones, especially of the back and leg, occurs In combination with the high blood calcium and low phosphorus, the above findings indicate a careful investigation of the parathyroid area for tumor or hyperplasia. Operative removal and the proper after-care, with the administration of **parathyroid extract** and, later on, of **calcium** preparations, usually assures successful treatment

D Hunter (Proc Roy Soc Med 24 486, 1931) reports a case in which *generalized osteitis fibrosis* existed in association with *hyperplasia* of the right superior *parathyroid* and *hyperparathyroidism* The tumor was removed and tetany prevented by a high **calcium** diet, intravenous and intramuscular **calcium**, **parathyroid extract** and irradiated **ergosterol**. General improvement was obtained in this case

A review of 11 cases of *bone changes* related to the parathyroid glands reported in the literature has been made by E L Compere (Surg Gynec Obst 50 783 (May) 1930) All the cases were characterized by pain, bowing of the weight bearing extremities, generalized osteoporosis, progressive weakness and general lassitude The blood chemistry of all cases was interesting and indicated, as was to be expected, an increase in the serum calcium, a decrease in serum phosphorus and a negative calcium balance Improvement was noted

in all cases in which ultraviolet light and a diet rich in **vitamine D** was given

Four cases with similar symptoms, blood chemistry and results from surgery are reported by J D Boyd, J E Milgram and G Stearns (J A M A 93 684 (Aug 30) 1929) Recently, Albright and Ellsworth reported a case which was diametrically opposite those mentioned above, *ie*, one in which *hypoparathyroidism* existed This case was also quoted by J de J Pemberton and K B Geddie (Ann Surg 92 202 (Aug) 1930) who report one of their own of *hyperparathyroidism*

The clinical difficulties surrounding the differentiation of *hypoparathyroidism* from *hyperparathyroidism* is described by J C Meakins (Canad M A J 24 654 (May) 1931) The former is characterized by a low serum calcium, a positive calcium balance and great tonic and hyperexcitability of the neuromuscular system The latter is characterized by a high serum calcium content, a negative calcium balance, a tendency to hypotonicity and hypoexcitability of the neuromuscular system with a pronounced rarefaction of the bones

The treatment of *parathyroid insufficiency* from a postoperative standpoint is ably discussed by W M Boothby, S F Haines, J de J Pemberton (Am J M Sc 181 81 (Jan) 1931) They have controlled tetanic spasms, including the laryngeal form, by a generous teaspoonful of **calcium lactate** in water every 2 hours In more severe cases 5 to 6 teaspoonfuls may be given by proctoclysis Intravenous calcium or parathormone extract is seldom necessary, according to the authors They warn against the danger of the use of large doses of **parathormone** over a long period of time and recommend that not

more than 5 to 10 units every other day be used

**PARATHYROID ORGANO-THERAPY.** See ANIMAL EXTRACTS

**PARKINSONISM.** See BASAL GANGLIA

**PARTURITION.—FORCEPS**  
—Although the conservative use of forceps is a means of saving the lives of many infants, nevertheless, the fetal mortality is higher than is usually appreciated, according to H J Stander (Johns Hopkins Hosp Bull 47 323 (Dec) 1930) Low forceps constitute over 80 per cent of all forceps deliveries, while high forceps was performed in less than 2 per cent of the cases Uterine inertia or prolonged second stage of labor accounts for over half the forceps operations Forceps delivery occurred 4 times more frequently in primiparous patients

Contracted pelvis occurred more than twice as frequently in the negro as in the white patient The gross fetal mortality incident to forceps deliveries is 10 per cent The fetal mortality in negro primiparas is 17.4 per cent, and constitutes the most important single factor in the production of the high gross mortality

The fetal death rate is definitely increased by failure of rotation in posterior presentations and is particularly high when the head is arrested in deep transverse

The duration of labor is a very important factor in increasing the fetal mortality incident to forceps delivery After 48 hours the fetal death rate becomes excessively high

Only one-fifth of all patients delivered by forceps had no perineal lacerations As tears are far more frequent in prim-

iparas, primiparity may be an argument in favor of routine episiotomy Experience shows that the negro is about twice as poor a risk as to both morbidity and mortality as the white patient.

The cephalic application of the forceps is preferable, as the high incidence of posterior and deep transverse presentations makes a pelvic application inadvisable

**PERCAINE.** See ANESTHESIA

**PERIMETRY.—BLIND SPOT.**  
—H S Gradle and S J Meyer (Am J Ophth 12 802 (Oct) 1929) discuss the pathological significance, size, location, and various methods of measuring the blind spot They are of the opinion that the portion of the optic nerve which lies in the canal is not subject to extension of disease from the sinuses by its relation to them, but by its relation to the soft tissues in and about the canals

H Wentworth (*Ibid* 14 889 (Sept) 1931) studied the blind spots of 200 normal persons under standardized conditions With a 1 degree test object the areas varied, from 6.8 sq cm to 17.5 sq cm, the average being 11.4 sq cm at 33 cm from the eye Wentworth regards the distribution of the blind spot more significant than its average size as a standard for diagnostic comparisons

**FIELDS.**—From their study of the factors that affect the size and shape of the *form field*, C E Ferree and G Rand (*Ibid* 14 1018 (Oct) 1931) conclude that variation in brightness affects the size of the field more with small than with large stimuli They recommend that form stimuli be used only until the level of visibility of the color stimuli is reached Beyond this point the color stimuli are more convenient and possess a special and perhaps differential susceptibility to pathological disturbances.

W D Rowland and A W Rowe (*Ibid* 13 413 (May) 1930) are of the opinion that, in order to determine the cause of *concentric contraction of the visual fields*, it is necessary to investigate the patient's health in general and his internal secretions in particular. In about 1000 of approximately 2000 cases examined they found a definite endocrinopathy and believe that, in order of frequency, the pituitary, the thyroid, the gonads, and other endocrines play an important rôle.

**ANGIOSCOTOMETRY**—John N Evans (*Ibid* 14 772 (Aug) 1931) believes that color fields have no clinical significance and that if a sufficiently small test object (0.5 mm) is used, every relative scotoma can be shown to be a positive defect. He has found angioscotometry helpful in glaucoma, focal choroiditis, retinitis, retrobulbar neuritis, vascular accident of the retina, and increased intracranial pressure. He routinely maps the fields of patients whose vision cannot be corrected to 6/4 provided there is no other evidence of disease to account for the reduction in vision.

**PERINEPHRIC ABSCESS.**  
See KIDNEY.

**PERNOCTON.** See ANESTHESIA,  
BASAL.

**PETROLATUM, IRRADIATED.**—The value of irradiated vaseline was accidentally discovered when this preparation was first used to fill up a sinus following an intestinal operation. Later, it was used in pustular conditions of surgical origin. The author believed its virtue to be due to vitamin D, however, on mixing petrolatum with viosterol, the results were therapeutically negative.

E H Eising (*Ann Surg* 93 1231 (June) 1931) considers that the stearols or the oleates treated in a similar way would be likewise beneficial and there seems to be a scientific basis for the favorable clinical results that have been obtained in its therapeutic use.

From the therapeutic standpoint, it has been found that most of the vegetable oils contain an acrid acid, such as oleic or stearic, which is offensive to the tissue, whereas the mineral oils are bland and inoffensive, even when inspired in a vaporized condition.

Ultraviolet light is one of the most potent means of atomic dissociation or ionization and this is, without doubt, what occurs when petrolatum or other substances are irradiated. Atomic dissociation is the forcible tearing asunder of the atomic structure of the molecule by striking off electrons from their molecular orbit and joining to the altered molecule a new speed of molecular vibration. It is quite conceivable, therefore, on the basis of electron physics, that any susceptible molecule can be rendered radio-active, and this seems to be the case.

The fact that irradiated petrolatum emits emanations which will penetrate a transparent material of the density of x-ray film, together with the fact that irradiated petrolatum will cause a wide divergent shadow to be caused by an object lying upon a photographic plate film, led the author to the conclusion that the emanations emitted from irradiated petrolatum are truly electromagnetic in nature. In conclusion, referring to the therapeutic value of irradiated petrolatum, Eising states that he believes the therapeutic virtue of irradiated petroleum resides in a secondary radiant energy endowed by its exposure to the ultraviolet light.

**PETROSITIS.**—The recent otologic literature refers to the *syndrome petrositis*, which is an involvement of the petrous portion of the temporal bone, and which occurs in the course of an acute mastoiditis. The infection from the tympanum reaches the petrous bone in various ways, depending a great deal on the pneumatization that is present around the labyrinth and in the petrous apex. The pathway of the infection may be either by direct extension through the perilabyrinthine cells—and this is commonly seen in the highly pneumatized temporal bone—or by way of the blood stream. The latter course is seen in those cases where the petrous apex is marrow-containing in character. The osteitis or osteomyelitis in the petrous bone may break through the cortex and produce a subdural abscess or meningitis, etc.

To appreciate more fully the development and course of a petrositis, the understanding of the anatomy of the petrous bone is necessary and since an involvement at the apex results in the classic *Gradenigo syndrome*, the knowledge of anatomical details becomes essential. Since all of the parts of the temporal bone, *viz*, the squamous, zygomatic, mastoid and petrous contain air cells, it will be readily seen that the highly pneumatized temporal bone is liable to have an involvement of the perilabyrinthine cells as well as those in the mastoid. Quite often the mastoid cells are thoroughly exenterated in a simple mastoidectomy and the patient fails to recover because of smouldering infected cells medially in the petrous bone. Should the pyramid also contain dehiscences, this adds to the ease with which a subdural abscess or meningitis is formed. It is unnecessary for the infection to involve the whole petrous

pyramid before an intracranial complication becomes manifest, since the infection can break through the bony cortex before it reaches the apex. This fact explains the many intracranial complications due to petrositis without involvement of the sixth nerve.

Between the apex of the petrous pyramid and the posterior clinoid process and sphenoid body is a space, which, with the petrosphenoidal ligament above, forms the abducens or *Dorello's canal*. The canal contains the abducens nerve and inferior petrosal sinus, which pass through it to enter the cavernous sinus higher and farther forward. The sixth nerve is in close proximity to the Gasserian ganglion in this area. The course of the abducens nerve is not constant. The proximal portion of the sixth nerve in Dorello's canal is accompanied by the inferior petrosal sinus, whereas on emerging it is found to be in close proximity to the Gasserian ganglion and the superior petrosal sinus. Therefore, in *Gradenigo's syndrome* the amount of facial pain depends on the location of the irritation of the sixth nerve, whether it is farther away from or nearer to the ganglion.

Inflammation reaches the apex in a highly pneumatized bone in various ways. H. J. Profant (Arch Otolaryng 13:347 (Mar) 1931) describes 2 routes from dissected specimens: (1) The antrum-epitympanic route. The cells extend from the antrum and epitympanic space above the cochlea, and above and behind the superior semicircular canal; then behind, above and in front of the internal auditory meatus, and finally to the mass of cells under the tegmen of the anterior surface of the tip. (2) The hypotympanic route. The cells extend from the hypotympanic space below the cochlea, then just below the internal

auditory meatus, and finally to the mass of cells under the tegmen of the posterior surface of the tip. Dissections of other pneumatic petrous bones showed that the cells can always be traced to one of these 2 groups. The author calls attention to the fact that from a clinical and surgical standpoint the important thing to bear in mind is that the infection may extend from the hypotympanic space, as well as from the antrum and epitympanic space. The presence of a petrositis must be considered when there is a recurrence of a profuse discharge after the mastoid cells have been thoroughly exenterated. Also in petrositis pain may be very pronounced, due to irritation of the fifth nerve. The pain is often referred to the region behind the eye on the involved side and over the temporoparietal region.

In many cases Gradenigo's syndrome is a complication of petrositis; the syndrome appears prior to mastoid operation or occurs subsequently to mastoidectomy. Pain in the temporoparietal region with paralysis of the external rectus muscle in the course of an otitis media on the affected side is the classic picture observed in this clinical entity. A petrositis can occur without Gradenigo's syndrome and the syndrome may be associated with other complications such as labyrinthitis.

**TREATMENT.**—The treatment of petrositis depends on whether or not the disease is progressive, such as the development of meningeal signs. W. P. Eagleton (Archiv Otolaryng, 13:386 (Mar) 1931) discusses the indications of surgical intervention in complications secondary to suppuration of the petrous apex. He described the technic of operation of unlocking the petrous pyramid and reports 4 cases with recovery in 3.

The treatment of Gradenigo's syn-

drome is conservative. Some patients have recovered after a myringotomy and the majority recover after a thorough simple mastoidectomy. In a non-progressive case the radical procedure of operating on the petrous apex is not indicated.

**PERTUSSIS.** See WHOOPING-COUGH

**PHENOBARBITAL.** See ANESTHESIA, BASAL

**PHENOL IN DERMATOLOGY.**—From an investigation by I. A. Matuissis and A. N. Pavlov (Arch Dermat and Syph 21:1002 (June) 1930) it was found that staphylococci die within 20 to 25 minutes when 1 per cent phenol solution is applied, within 10 minutes with 1.25 per cent aqueous solution and within 5 minutes in 1.5 per cent solution. Solutions of phenol in alcohol and oil do not possess any disinfectant properties, whereas these are increased by common salt and other salts. In 486 cases a 3 per cent solution of phenol was used by injection into the external upper quadrant of the buttocks. Beginning with 1 cc, the second injection was 2 cc and the third 3 cc of the solution, 3 cc being continued every second day until 15 to 25 injections were given.

Traces of phenol were found in the urine 25 minutes after injection and could be identified 18 hours afterward. It is excreted by all the mucous membranes.

**PHRENIC NERVE SURGERY.**—This method of securing rest of the involved lung is meeting with greater acceptance. The gradual gain in favor of these procedures can be attributed to



the appreciation of an economic as well as a therapeutic value. From the standpoint of economy, and this must of necessity be given consideration, J. Alexander (Ann Int Med 4 348 (Oct) 1930) indicates its value in that a single procedure replaces the numerous injections needed for pneumothorax. The average simplicity makes it available wherever pulmonary tuberculosis can be adequately treated, whether in sanatorium, metropolitan area or less dense center of population. The local detailed anatomic knowledge requisite is available to all competent to do surgery. M. Tapis (Rev Espan de Tuberc 1 25 (Apr) 1930) speaks of its value where social conditions prevent pneumothorax.

As with all pulmonary surgery in tuberculosis, it must be considered only as an adjuvant rest measure, and at no time may be considered as justification for relaxation of any particulars in treatment.

**INDICATIONS.**—The indications for its use vary widely in the minds of different operators, but with an increasing tendency to its earlier use in the practice of broadly experienced men. E. J. O'Brien (Arch Surg 21 1134, pt 11 (Dec) 1930) says "It is a benign lesion indeed in the treatment of which I do not feel that at least a crushing should be resorted to in order to give the patient the additional rest offered while the diaphragm is paralyzed." S. E. Hughes, Jr (Virginia Med Monthly 57 311 (Aug) 1930) also speaks favorably of the temporary interruption secured by crushing in early and minimal lesions.

Contrasted with pneumothorax, it is recognized that the collapse obtained by phrenic operation is not nearly so complete, investigations by O'Brien (*loc cit*) showing that following phrenicectomy,

there was an immediate decrease of about 32 per cent in the vital capacity of all patients. This reduction, however, is not equally distributed throughout the volume of the lung on the side of the operation. R. W. Matson (Am Rev Tuberc 22 1 (July) 1930) states that the results of an induced hemidiaphragmatic paralysis are less dependent upon the site of the lesion than upon its type. This is explained by the fact that in certain types of tuberculosis, particularly the proliferative varieties, the capacity of the diseased lung for contraction is greater than that of healthy lung tissue. Therefore, even though the lesion is in the upper lobe, the rising diaphragm, by reducing the volume of the hemothorax, permits the collapse capacity of the diseased lung tissue to exert itself, even without any collapse of the healthy lung tissue. The writer's belief that in the productive types of tuberculosis the collapse capacity of the diseased lung is greater than that of healthy tissue is based upon years of observation in pneumothorax therapy, during which he has observed that in the absence of adhesions, the diseased lung tissue almost invariably collapses before healthy lung tissue. As a matter of fact, the writer states, in some cases observed over a period of many years the healthy lung tissue has always been in contact with the chest wall, the diseased tissue alone being collapsed. O'Brien (*loc cit*) has noted that there is, as a rule, a greater tendency to contraction in the diseased area than in normal lung tissue, and he states that he has often obtained a selective collapse without much loss of alveolar function.

As with many relatively recent surgical procedures which appear radical because lacking the sanction of long usage, operative work was first ven-

tured in the advanced cases showing little evidence of limitation under accepted purely medical measures. Consequently, most of the conclusions now available on indications for phrenic nerve surgery are based on cases the seat of long standing pathology, but since large numbers of patients will still progress to late stages of disease before reaching a point where some attendant will entertain the idea of surgical treatment, the analyses of early surgical experiences are of value.

Primarily, because the seat of change in pleural capacity takes place in the lower thorax, it was first thought that basal lesions were particularly amenable to this treatment. Confirmation of the truth of these deductions is given by J D Brooks (U S Vet Bur M Bull 6 1042 (Dec) 1930) and by L W Frank and O O Miller (Ann Surg 91 669 (May) 1930), who find that basal and midlobe lesions offer most promise of improvement. Agreement with such conclusions is held by F Oeri (Schweiz med Wchnschr 61 131 (Feb 7) 1931) and by E S Welles (Arch Surg 19 1169 (Dec) 1929). But, as already indicated, the actual pulmonary collapse is greater in the involved area of proliferative pathology than in healthy lung tissue, so that there can be accepted much broader indications for use than only in cases of unilateral basal involvement, and these are summarized by Matson (*loc cit*) as follows: It is strongly recommended in all patients for whom a pneumothorax is indicated, and adhesions prevent the introduction of gas; where thoracoplasty was contraindicated because of the state of the contralateral lung; as an independent procedure in those cases in which a thoracoplasty is impossible, and as a preliminary to every thoracoplasty.

The existence of considerable disease in the contralateral lung is not taken as a contraindication unless the disease is far advanced in both lung fields, or many surgical complications exist. Obviously collapse of the lung should not be instituted if the fields of both lungs are so involved with disease, and the vital capacity is so low that the patient's respiratory ability might be endangered. It is advisable in bilateral tuberculosis, however, to begin collapse therapy on the side most affected, as this alone is often sufficient to cause healing in both lungs. O'Brien (*loc cit*), L Bernard and G Poix (Press méd 39 201 (Feb 11) 1931) believe that phrenicotomy alone is likely to succeed where there is a marked tendency to fibrous contraction.

**TECHNIC—Dangers.**—The technic of phrenic exeresis has been established by Felix, and is successful in the large majority of cases. Explanations of failure to uniformly secure permanent hemidiaphragmatic paralyses by the simple section of the nerve are made by the studies of R C Matson and A Plenk, which confirm Felix's findings of a large percentage of anatomic variation in the origin and exact course of the phrenic nerve. The dissections of these investigators revealed a variation in 28 of 112 cadavers from the commonly accepted anatomic formations. In a small number of cases such gross anomalies as double phrenic trunks or unilateral or even bilateral absence of the typical trunk on the anterior surface of the scalenus was noted. The greater percentage of variation was in the source and course of the accessory phrenics. This at the same time is the most valuable part of their contribution, explaining failures where even a considerable length of nerve is extracted.

Accessory fibers arise most commonly from the fifth cervical, either near or with the nerve to the subclavius muscle. If arising with the nerve to the subclavius, the accessory fiber usually separates from it just before the nerve to the subclavius enters the muscle. The accessory branch then continues downward, passing in front of the subclavian vein, to join the main stem of the phrenic just behind the sternal end of the first rib, a point about 10 to 12 cm below the usual site of operation. The operator may feel confident of complete interruption of all impulses if 10 to 12 cm of nerve have been evulsed.

As practical application of the information obtained Matson further states that when the section of nerve fiber evulsed measured less than 10 cm, the operation was converted into the radical phrenicectomy of Goetze by resecting a small section of the nerve to the subclavius as well as all communicating fibers. He gives the histories of 11 cases in which the trunk removed measured less than 10 cm, and in which the Goetze technic was not followed. In 3 of these 11 cases the diaphragmatic function returned in less than 6 months, although hemidiaphragmatic paralysis was shown immediately after operation. Having observed no case of return of function where 10 cm or more of nerve had been removed, he concluded that a return of diaphragmatic function can be expected in about 25 per cent of cases if accessory and communicating branches are not sought for and severed where less than 10 cm are extracted by evulsion.

Simple as the operation may appear to be, it is, unfortunately, not without danger. Primary dangers are associated with the area of the operation field, involving as it does one containing closely

approximated vital nerve and vascular structures. Care and patience in dissection will avoid such pitfalls, though recently E. S. Welles (*loc cit*) has added another instance of severance of the thoracic duct to those already reported.

Matson (*loc cit*) quotes reports from the Sauerbruch clinic, of vascular injury requiring ligation of the subclavian artery, and of venous channel laceration resulting in fatal and in nonfatal embolism. Confusion of nerve structures in the operative field with damage to the sympathetic and vagus, are reported in the same article.

Beyond the visible operative field lie possible dangers associated with nerve anomalies or with the pathologic process itself. F. B. Berry (*Arch Surg* 21:1125 (Dec.-pt. 11) 1930) gives consideration to these aspects in an article on "The Unfavorable Results of Phrenicectomy." From a compilation of statistics covering 4697 cases from worldwide sources, he finds 57 cases of complications directly attributed to the operation itself, 26 of which were fatal, and which in the remaining 31 produced a distinct aggravation of the pathology. The most terrifying of these complications, because not remediable, are the immediate mediastinal hemorrhages, supposedly due to tears of the pericardiophrenic artery. Matson (*loc cit*) states that the danger of tearing into the subclavian vein must always be considered, since the accessory branch usually wraps around the subclavian vein to join the main stem of the phrenic. If this accessory branch is large or firmly attached to the main phrenic, there is danger of tearing into the veins. Matson and Plenk, in their dissections, discovered an accessory fiber coursing through the wall of the subclavian vein,

and it has been reported as passing directly through the subclavian vein

Mediastinal adhesions are probably responsible for pneumothorax followed by ultimately fatal empyema, and for mediastinal empyema, also fatal, found in Berry's list. Pulmonary embolism, pulmonary edema, persistent tachycardia, fatal respiratory insufficiency and asphyxia from pulmonary flooding by secretions from the collapsed side are also here reported. Other fatalities have been assigned to a prompt spread of the tuberculous process or to the development of atelectasis and later pneumonic sequelæ

It is the knowledge of such possibilities that prompted T. Naegeli and H. Schulte-Tigges (München med. Woch. 77:2061 (Nov. 28) 1930) to caution that the simple technic of this method should not be a temptation to perform it without carefully evaluating its advisability

With such possible anatomic and pathologic basis for tragic complications, certain cautions in the actual technical procedure are worthy of observation

Berry (*loc. cit.*) advises that whenever the nerve cannot be readily drawn up from the mediastinum, or where chronic mediastinitis is recognized or suspected, he is always satisfied with a moderate resection of the nerve such as may be obtained without undue traction. Matson (*loc. cit.*) finds that in still another group of cases the nerve is so densely adherent in the mediastinum that evulsion is impossible. The nerve either breaks (the distal end retracting into the thoracic cavity) or the operator is forced to cut it because of the fear of damaging important structures

*Psychic disturbances*, as after any operative procedure in the physically handicapped, may be seen. Tachycar-

dia and dyspnea are easily understood and, fortunately, seldom serious complications. Of much interest are the digestive disturbances usually only temporary, but occasionally persistent, especially in left side cases, where by unusual rise of the diaphragm, with ascent of the cardiac end of the stomach, a gas-trapping takes place in the fundus because of the elevation of that part of the organ above the level of the esophagus

**END-RESULTS.**—Time is a necessary element in evaluating results, likewise a uniformity in classification, in order that the inquiring reader may have sufficient information on which to base conclusions. It is for these reasons that the already quoted report of Matson particularly appeals. He reviews 66 cases of the productive type of tuberculosis, in which a pneumothorax was attempted and failed because of pleuritic adhesions. All of these patients were suffering from far advanced tuberculosis (N. T. A. III). Most of them were experiencing an acute exacerbation of their disease and were therefore actively febrile and suffering from marked loss of weight and strength. With 1 or 2 exceptions, all cases had demonstrable excavations on the operated side; in many cases a large cavity of 4 to 5 × 6 to 8 cm. was present. In all cases the disease exhibited the characteristics of an upper lobe lesion, even though the entire lung was involved. No distinctly lower lobe lesions are included

In 34 cases of the 66, a thoracoplasty was contraindicated because of the state of the contralateral lung (active or progressive disease). In this group of 34 such cases, 18 (52 per cent) have been listed much improved which, according to the criteria demanded by Matson for

such classifications, means that they have become bacillus free, as demonstrated by concentration methods, have gained weight, are free of subjective symptoms, and are able to carry on occupational activities. An additional number (12 or 38 per cent) are rated as "improved," meaning less sputum, mostly afebrile, many resuming occupational activities, but all still sputum positive. The remaining cases—10 per cent of the total, are rated unimproved or made worse.

In 32 cases of the 66, of "essentially unilateral disease," in which thoracoplasty was considered as indicated, and the operation of phrenic exeresis done as a preliminary to the major procedure, there was such improvement in 11 (35 per cent) that thoracoplasty became unnecessary. In this group of 11 cases the same criteria were fulfilled without further surgery as in the group marked "much improved" above.

In the whole group of 66 cases, 42 per cent have become bacillus free, a truly positive evidence of the value of the surgical procedure in a number of patients showing steadily advancing pathology in spite of careful medical treatment. L. Graf (*Beitr z Klin d Tuberk* 74 221 (June 23) 1930) reports on 67 patients (almost exclusively cases with cavitation) who have been under observation from 2 to 6 years. Of the group 62.5 per cent are bacillus-free and 53.5 per cent are able to do their regular work. This is a confirmation of the above.

Because of the experience of F. Bertatto and R. Dal Lago (*Semana méd* 2·1579 (Nov 28) 1929) phrenicectomy is to be considered in *recurrent hemoptysis* where pneumothorax cannot be instituted. Their report covers 2 cases in which marked hemostatic effect

was obtained in spite of inability to lead sedentary lives, and in the presence of some involvement of the other lung in addition. Matson (*loc cit*) found that in 2 cases a serious hemoptysis which was threatening the life of the individual ceased immediately after operation. Alexander (*loc cit*) also speaks of the value of temporary paralysis as obtained by crushing in cases of hemoptysis.

**BILATERAL PHRENICOTOMY.**—Clearcut indications for and against this procedure have not been recognized. L. Dunner (*Deutsch med Wchnschr* 55 1918 (Nov 15) 1929) speaks of varying results. He believes that it should not be attempted where the thorax is rigid because of the possible insufficiency of costal breathing, nor if, after exeresis on one side, the diaphragm stands abnormally high.

**PHYSIOTHERAPY.**—In commenting on the use of physical therapy in the treatment of infirmities, P. Roth (*J Michigan Med Soc* 28 843 (Dec) 1929) states that it is the method of choice wherever possible and that chemical and medical agents should be used only when physical therapy fails.

R. Kovacs (*Med J and Rec* 133 105 (Feb 4) 1931) states that every physician, who wishes to do justice to his patients, should be familiar with various physical therapeutic agents such as baths, massage, electrical therapy, etc., and that if his own practice is so extensive that he cannot keep sufficiently informed on the subject, he should employ a skilled assistant. He also states that in 1929 over half of the general hospitals in the United States reported the establishment of physical therapy departments and that almost every orthopedic and mental hospital had such a department. He believes in the future

that it will be an integral part of all hospital treatment

M L H A Snow (Physical Therapeutics 49 65 (Feb ) 1931) feels that physical therapy has a very definite place in orthopedic treatment and that those physical agents best adapted to overcome noninfectious inflammation are hot dry air, x-rays, ultraviolet rays and diathermy. Those physical agents most valuable as sedatives are the radiant light and heat, infrared rays, and hydrotherapy. Those most fitted to overcome muscular tension are static wave current, the static sparks, mechanical vibration and the sinusoidal current. Other agents of value are massage, exercise and the static induced current.

E Duntzer and M Hellendall (Munchen med. Wchnschr 76 1835 (Nov. 1) 1929) correlate statistics which they collected on 1500 female participants in gymnastic contests. They concluded that gymnastics as such caused no marked change in the female pelvis, although in many cases the highly trained women were of a type which would naturally have a small pelvis. In most of their cases the women who had borne children had relatively easy labors. Many of the women continued exercise during pregnancy. They found that menstruation was not a contraindication to physical exercise except during extremely warm weather or cold weather, and where attempts were being made to set new records, at which time undue physical stamina would be required. They believe that the physical efficiency of women is slightly below par during the menstrual period.

In commenting on various types of physical therapeutic agents, H Wolfson (J A. M A 96 2019 (June 13) 1931) states that in certain physical therapeutic procedures, as heat and massage, an in-

creased blood supply is produced, due to active dilatation of the blood vessels. Electricity, on the other hand, does not increase blood flow, but clinically has been found to aid in the treatment of poliomyelitis and peripheral nerve injury, although the cause in these cases has not been ascertained. He feels that more frequent but shorter treatments of massage and passive motion are most advantageous.

The subject of physical exercise is discussed by A Abrahams (Practitioner 126 566 (May) 1931), who states that exercise which most appeals to the patient is the one which should be encouraged by the doctor. He does not feel that there is such a thing as being "burned out," but that athletes to whom this term is applied are really in a stage of retrogression from which they will recover and later improve if the exercise is persisted in. He feels that such a thing as cardiac strain is not a satisfactory explanation for cessation of athletic endeavor and states that in most cases the heart withstands the violent exercise where the weaker organs of the system give way. He believes that it is nothing short of criminal to keep growing boys and girls away from athletic competition, as such restraint gives them a psychological aspect which makes them unfitted for companionship with their fellow men.

**PIGMENTATION OF THE SKIN.**—In calling attention to the clinical and histopathologic features, and to the differential characteristics of the increase in pigmentation of the skin in Addison's disease, acanthosis nigricans and hemochromatosis, Hamilton Montgomery and P A O'Leary (Arch Dermat. and Syph 21 970 (June) 1930) state that pigmentation is due to



(1) increase of melanin, (2) deposit of heavy metals, (3) deposits of extraneous pigments, and (4) vascular disturbance

Microscopic study is essential in analyzing pigmentary disturbances. If pigment is absent from the epidermis and there are melanin deposits in the cutis the clinical appearance of the skin will be blue rather than brown. The "blue nevus" of Jadassohn is an example. Deposits of hemosiderin from hemorrhage present a steel blue color clinically difficult to distinguish from early melanoepithelioma. The darker races have more deposits of melanin in the skin.

In *Addison's disease* due to disease of the suprarenal glands the hyperpigmentation occurs essentially at the sites at which pigmentation is normally increased—the flexural folds, such as the axilla, groin, perineum, umbilicus and beneath the breasts—sometimes almost black. There is usually pigmentation of mouth, anal cleft, vagina and areola of the nipples. Exposed parts and points of friction are affected. The texture of the skin is unchanged, but there is a marked increase of melanin in epidermis and cutis, especially in the basal cells and tips of the rete ridges.

*Acanthosis nigricans* is rare and is divided into (1) juvenile type and (2) adult type. The first is of unknown origin, but has been attributed to both tuberculosis and endocrine disturbances. It apparently does not interfere with general health. The second type is generally associated with primary or metastatic neoplasm of the abdomen and the typical picture develops when the chromaffin system of the celiac plexus is involved through extension or pressure.

The areas of pigmentation are the

same as in Addison's disease, but, in addition, there are hyperkeratosis, and verrucous and papillomatous lesions in the pigmented areas. The pigment is melanin and may show in the mouth. At the beginning it may be impossible to distinguish from Addison's disease, the microscopic picture, however, is usually typical and even diagnostic. It shows relative and positive hyperkeratosis, marked irregular acanthosis, elongated narrow papillary bodies and dense melanin pigmentation of the basal cells of the epidermis.

*Hemochromatosis* is characterized by deposits of hemosiderin in various organs, including the skin and is usually seen in diabetes and cirrhosis of the liver. The pigmentation is diffuse and occurs chiefly on exposed surfaces and sometimes on mucous surfaces. The skin changes to a color composed of grey, blue and brown, according to the amounts of hemosiderin and melanin present. Microscopically, the skin is unchanged except for the deposit of pigment. Hemosiderin was always to be found in the propria of the sweat glands and often about the blood-vessels.

**PINEAL GLAND.—TUMORS AND CYSTS.**—M. Balado and R. Carrillo (Arch. argent. de neurol. 4: 167 (May) 1929) report a case of *cyst* of the pineal gland in a boy aged 12 years. He had progressive loss of vision for a period of 2 years, ending in complete blindness. For 10 months he experienced difficulty in walking, always tending to fall toward the right. For 4 months he was unable to walk at all, and for 26 days he had been somnolent. Conjugate deviation of the head and eyes to the right with convulsions also occurred. He had marked

headache and vomiting, with catatonia for a period as long as a quarter of an hour. Passive movements were normal except for slight rigidity.

A cystic tumor originating in the pineal gland was revealed at operation. Death occurred on the twentieth day. The lesion involved the hypothalamic and red and black nuclei and pressure was present on these centers. The cyst was eccentric in its growth and lined by cells of a pineal tumor. Lesions of the myelin fibers caused spasticity of the lower limbs. Attacks of risus nocturnus were probably the result of a destruction of the right corpus striatum.

A similar case in a boy, aged 11, is described by F. Altmann (Wien klin Wchnschr. 43:108 (Jan 23) 1930). He was thoroughly studied and roentgenoscoped, and diagnosed as internal hydrocephalus, plus a calcified tumor of the pineal body. The boy died and histologic section of the tumor revealed it to be a *dermoid cyst*. All forms of tissue, including epithelium, connective tissue, hairs, fatty, osseous and cartilaginous tissues were found. The internal hydrocephalus was probably the result of pressure on the cerebral aqueduct.

A detailed report on *pinealomas* is given by J. H. Globus and S. Silbert (Arch Neurol and Psychiat 25:937 (May) 1931) in which they describe tumors of the pineal region in a group of 7 cases. All were examples of the single type of new growth. The identification of the true character of this type of neoplasm is aided by a study of the pineal gland through its various stages of development. The gland, according to their study, revealed several critical histogenic stages which are duplicated by the histologic picture and structure of the tumors of

this region. With the recognition of the transitions in the development of the pineal gland, according to the authors, it is possible to assemble the majority of the tumors of this region though diverging in histologic structure into a single group. They have definitely established by their observations the fact that such tumors are autochthonous *teratomas*. The absence of glial or neuroglial constituents during the evolutionary stages of the pineal body excludes the existence of spongioblastic or neuroblastic forms of pinealomas. The 7 cases reported by the authors reveal no new or unusual clinical features, but add further evidence of the fact that manifestations of increased intracranial tension, indicating involvement of the structures in the periaqueductal region, justifies a diagnosis of tumor in the region of the quadrigeminal plate. Finally, the authors point out that the occurrence of alterations in the secondary sexual characteristics is not essential for the diagnosis of pinealoma.

**Surgical Treatment.**—W. P. Van Wagenen (Surg Gynec Obst 53:216 (Aug) 1931) has described an approach to the pineal gland in cases of tumor, situated in this area, by means of a subcortical incision in the temporal area. This may be described as follows. A reversed L-shaped incision from 6 to 7 cm long was made in the cortex extending from the posterior end of the superior temporal lobe gyrus, upward and slightly backward to the lobulus parietalis superioris. The incision was carried downward into the ventricle with the aid of the electrocautery without difficulty. Wet cotton pledgets were placed over the exposed choroid plexus and in the opening of the ventricles to keep out blood and tumor débris. The author believes that

the choroid plexus should not be covered with cotton, as considerable bleeding followed removal of the cotton at the end of the operation. The thin medial wall of the lateral ventricle was incised with the electrocautery and the third ventricle was opened anterior to the tumor. The tumor, which was about 3 cm in diameter, lay between and above the large dilated *venæ vorticosæ*. At its base it was adherent to the tributaries of the vein of Galen in the case which he described. Practically all of the tumor, except a small bit adherent to large veins, was removed.

For 24 to 36 hours after the operation, the patient had a Biot type of respiration and weakness of the left side, and 48 hours after operation she was comatose. The wound was then opened and a drain inserted into the incision in the cortex, when her condition rapidly improved. Blood tinged spinal fluid and a small amount of tissue debris were removed. The weakness on the left side cleared up and the strength of the 2 sides is now normal. A left homonymous hemianopsia persisted, however, and there is slight hypesthesia to pinprick over the left side and, at times, an astereognosis on the left for test objects. Fifteen months after operation the patient was able to return to work. The neoplasm proved to be a spongioblastic type of tumor of the pineal gland.

#### PITUITARY GLAND.—EXPERIMENTAL PHYSIOLOGY.—

L Kraul (Am J. Obst. and Gynec 21 301 (Mar.) 1931) obtained pituitary glands from rabbits, guinea-pigs, mice and rats which were treated with placental extract, placental tissue, corpus luteum hormone, folliculin and urine of pregnant women, and implanted them

into mature mice. More lutein tissue and a greater number of pseudocorpora could be seen in the ovaries of such mice than in those obtained from animals in which normal pituitary glands had been implanted.

Follicular growth promotion by the pituitary glands of animals treated with folliculin or placental tissue was variable, but occasionally increased. Placental extract, corpus luteum hormone and urine from pregnant women had a less pronounced effect. Injections of suprarenin did not cause an increase in the luteinization of pituitary gland in transplant. Implants of the placenta of guinea-pigs, cats and rats into immature mice only had a slight effect on the ovaries.

X-ray radiation of the head had no effect in increasing the luteinizing power of the pituitary gland. On the other hand, the pituitary glands of the animals whose ovaries had been previously irradiated caused a distinct luteinization of the ovaries of immature mice.

The continuous administration of corpus luteum hormone, placental extract or tissue, folliculi and the urine of pregnant women to adult rabbits, guinea-pigs, rats and mice caused a luteinization of varying degree attended with the alteration or suppression of the ovarian cycle.

The anterior pituitary gland, according to the author, does not store hormones. The human placenta at term does not contain corpus luteum hormone. That the yellow body has a certain degree of independence of the ovum, is evident from the fact that it continues to function after removal of the ovum.

By the use of extracts of the anterior pituitary body, various investigators have shown that the anterior pituitary

body contains 2 hormones which act on the ovary. One stimulates the development of the follicles and the other activates the lutein tissue. In this article the author shows that the whole gland can produce both effects.

The anterior pituitary body itself is influenced by endocrine substances of the ovary and placenta. Consequently it does not absolutely control the ovarian cycle in itself. On the other hand, a cyclic function of the anterior pituitary due to this reciprocity is quite probable, although as yet not proved.

The author points out that it must be borne in mind that the injection or implantation of various substances may act on the ovary of the immature mouse directly or affect it only indirectly through its action on the pituitary gland of the test animal. This introduces the possible error in the inferences drawn.

C. E. Dodds (Proc Roy Soc (Sect Med) 23:1 (Dec) 1929) believes there are at least 2 and probably 3 hormones secreted by the anterior lobe. Leyton also has been under the impression that there were 2 substances elaborated from the anterior lobe of the gland and this has been confirmed by the production of an oxytocic and also a pressor extract from the gland. He also confirmed the opinion that the fresher extracts have given better results in diabetes insipidus and that filtering diminished the potency of the extract.

C. H. Frazier (Surg. Gynec. Obst 52:1069 (June) 1931) states that although the *interrelationship of the pituitary with other glands* is most varied, it is probably most constant with the thyroid. Thyroid deficiency causes a persistent and consistent hypertrophy of the hypophysis in the male, but not in the female. The growth response of the

pituitary to thyroid activity does not run parallel to the body response to growth. It has often been stated that the anterior lobe is the specific part which activates the thyroid. Partial extirpation of the thyroid and suprarenals in the parents will result in development of the pituitary to twice or 3 times its size in the offspring. There appears to be no specific growth relationship between the parathyroid and the pituitary glands. The author has observed that one of the earliest symptoms of pituitary disease antedating all others by many years is amenorrhea. Impotence in the male is a symptom which usually develops after many others have made their presence known.

**SYMPTOMATOLOGY.**—Sixty cases of pituitary *headache* are reported by L. H. Mayers (Endocrinology 14:319 (Sept-Oct) 1930) occurring in women of a particular constitutional type, *viz*, obese, short-waisted, energetic, alert and intelligent, with definite menstrual disturbances. The symptom of headaches develops at puberty, immediately after marriage, or after childbirth, and is totally relieved by hypodermatic injections of pituitary extract.

The relationship of narcolepsy to pituitary disorder is discussed in 2 cases reported by Beyermann (Arch f Psychiat 91:463, 1930). Both cases showed small sella turcica, with bridging of the clinoid processes, and typical symptoms of hypofunction. The narcoleptic attacks cleared up under the administration of anterior lobe pituitary extract.

Graves (Proc Roy. Soc (Sect Med) 23:1 (Dec.) 1929) points out 4 symptoms in *mental* cases which seem to have a direct relationship to pituitary function, *i e*, (1) general loss of muscle

tone; (2) disturbances of the peripheral circulation, (3) disturbance of nutrition, and (4) disturbance of the reproductive mechanism

F Schellong (Klin Wchnschr 10 100 (Jan 17) 1931) described observations on 4 patients with *hypophyseal insufficiency*. He draws particular attention to a peculiar disturbance in the circulation which manifests itself in collapse and fainting. Many such cases have been reported, according to the author, in the cases of pituitary cachexia but they have never been completely explained. It was found by observation of the blood-pressure on these patients that it was somewhat depressed after exercise or mild activity rather than increased. The heart action did not show any changes. Even after the injection of epinephrin to elevate the pressure, it was reduced after a small amount of activity. This circulatory disturbance could be partially counteracted by the injection of extracts of the hypophysis. Thus the author concluded that the extract of the pituitary influenced the peripheral vessels. He believes that the phenomenon of a reduction in the blood-pressure is the result of either a reduction in the peripheral resistance or an abnormal dilatation of the vessels. Anatomic observations have proven that insufficiency of the pituitary gland influences markedly the other glands of internal secretion. Although fainting and collapse are often seen in suprarenal insufficiency, the author does not believe this to be an associated condition with the pituitary lesion because (1) the blood-pressure at rest is usually normal or sometimes even increased and (2) epinephrin is not active or effective in counteracting the regulatory disturbance.

**TUMORS.**—An interesting case report by H. M. Teel (Arch Neurol. and

Psychiat 26 593 (Sept ) 1931) of a *basophilic adenoma of the anterior hypophysis*, opens up a field of interest in the relationship of this gland to growth, secondary sex characteristics and the size and function of other glands of internal secretion. The patient, a woman of 20 years, had menstrual irregularity, obesity, marked growth of hair on the face, chest and abdomen, and a much enlarged thyroid gland. Death was due to meningococcic meningitis, but the main interest histopathologically was in the endocrine system. There was a basophilic adenoma in the anterior lobe of the pituitary, which is not a frequent occurrence. The thyroid, which was quite large, showed fibrous and involutional changes. The thymus was distinctly larger than normal and showed no evidence of involution. In the pancreas there was definite increase in the number of islets, the suprarenals were both enlarged and the ovaries considerably larger than normal.

The author calls attention to the enlargement of other endocrine organs when anterior hypophyseal substance is administered for a long time to animals and that gonadal hypertrophy is directly related to the basophilic cell content in the anterior lobe. This relationship had been predicted by H. M. Teel and H. Cushing (Endokrinologie 6:401 (June) 1930).

Tumors of the pituitary body were discussed by W. J. Adie, N. Dott, E. C. Dodds and H. Cairns (Proc. Roy. Soc. (Sect. Med.) 23:1 (Dec ) 1929), according to the staining properties of the cells. They were classified as granular and agranular adenomata. Adie believes that there is a rough agreement between the cell structure of the tumor and the symptoms, but no rigid formula could be devised. A large tumor may

cause failure of vision and not show glandular symptoms. Persistent glycosuria occurs with the granular adenomata only in the advanced cases. Treatment is better applied by an application of knowledge of the course of the disease. According to the authors, **surgery** is only indicated to relieve headache and conserve vision. In acromegaly **x-ray** therapy may be of value, but substitution therapy is not fully developed.

By far the most common and important tumor is *adenoma* of the anterior lobe with *acromegaly*. This is an agranular adenoma and the cardinal sign is loss of vision. When acromegaly is present it is usually associated with an agranular adenoma of this lobe.

The *diagnosis* of this lesion of the pituitary gland is most difficult and tumors should be suspected in all cases of failing vision when no definite cause is demonstrable. Tabes and pituitary tumor with progressive optic atrophy may be differentiated by the Argyll-Robertson pupil.

Diabetes insipidus is a most important manifestation of pituitary disease. Its exact mechanism is not thoroughly understood. It is known that the condition may arise from disease of the pituitary as well as the hypothalamus.

**Treatment.**—Dott (*Ibid.*) advocates **radiotherapy** for early adenomata and **surgery** for the relief of pressure when vision is impaired. He believes the transphenoidal approach to be the best for simple adenomata and the transfrontal approach for cases with intracranial expansion.

G. E. Pfahler and E. W. Spackman (*Am J Ophth* 14:796 (Aug.) 1931) state that pituitary tumors are more radiosensitive and more amenable to **x-ray** therapy than tumors elsewhere in

the head. X-ray therapy is usually followed by improvement in eye conditions subjectively and objectively. Records of the visual field, especially color fields, gauged the improvement. Polyuria, glycosuria and genital dystrophy also improved. Solid adenomas are more radiosensitive than the cystic forms. Six cases are reported in detail, of these, 3 were greatly benefited. They recommend high voltage x-ray treatment first in these cases, observation for 6 weeks to 6 months, and if there is insufficient response, **surgical intervention**.

#### PITUITARY ORGANOTHERAPY. See ANIMAL EXTRACTS

**PLACENTA.—NECROSIS.**—A study of 400 consecutively delivered placentas from the Jefferson Medical College Hospital was made by T. L. Montgomery (*Am J Obst and Gynec* 21:157 (Feb.) 1931). He concludes that necrosis of the placenta is a physiologic phenomena and is found partially in every full term placenta. A degeneration of the syncytium and deposit of fibrin in the intervillous space initiates the process. It is probable that with gestation, ferments are formed by the maternal tissues as a protection against the invasive character of the chorionic epithelium and that these ferments, as constituents of the maternal blood, cause syncytial degeneration.

Necrosis of the placenta is found no more frequently in toxemias than in normal pregnancy. The term necrosis is preferred to infarction, because the process begins with small areas of tissue death rather than with circulatory obstruction.

**PLACENTA PREVIA.**—C. H. Peckham (*Am J Obst. and Gynec* 21:39 (Jan.) 1931) found that in



a service of more than 36,000 admissions at Johns Hopkins Hospital, placenta previa occurred 146 times or 1 in 250. In emergency admissions the incidence was 1 in 30, whereas among those registered for prenatal care it was 1 in 500. It occurred once in every 98 deliveries in white patients and once in every 158 in negro women. The maternal mortality for the series was 11 per cent, being higher in the negro than in the white race (13.2 per cent as compared with 9.7 per cent). The maternal mortality from 1896 to 1910 was 19.2 per cent; since 1920, it fell to 8.6 per cent. In 57 marginal variety cases there was only 1 death (1.7 per cent), 14.7 per cent of the partial variety died, while central placenta previa gave a mortality of 21.4 per cent. In 33 women admitted with a pulse below 90 there was not a single death.

The highest death rate occurred in the group delivered immediately after admission, *ie*, 25.5 per cent. There was not a single death among 35 women who were delivered not less than 12 hours after admission. The death rate was only 4.5 per cent when the pregnancy ended before the last lunar month as compared to 15.5 per cent in those patients at term. The mortality rate was higher in multiparas and highest in women who had had 10 or more previous pregnancies. The highest mortality occurred in women of 40 or more. Infection caused only 1 death; hemorrhage was responsible for 13.

The gross fetal mortality was 67.8 per cent. This may be accounted for partially by the number of premature infants, as 43 per cent weighed less than 2500 Gm. If only those infants weighing 2500 Gm or over are considered with fetal heart beat present on admission, the mortality fell to 38.7 per cent.

**TREATMENT.**—A. H. Bill (Am J Obst and Gynec 21:227 (Feb) 1931) advocates **immediate hospitalization** for all cases of placenta previa, without previous vaginal examination or packing. In all cases of doubtful operative risk, prophylactic **blood transfusion** is indicated. If there is little or no cervical dilatation, **Cesarean section** should be performed regardless of the child's viability. In the marginal variety of placenta previa, however, if there is considerable dilatation and engagement of the fetal head, **rupturing the membranes** may control hemorrhage until the baby is delivered by forceps, or by **podalic version** if the head is high.

#### PLACENTAL ORGANO-THERAPY. See ANIMAL EXTRACTS

**PLASMA VOLUME DETERMINATION.**—The *carbon monoxide method* for the determination of plasma volume is considered by S. Graff and H. T. Clarke (Arch Int Med 48:808 (Nov) 1931) to be more reliable than the dye method. These writers use brilliant vital red, and oxalate the blood samples with 1 per cent sodium oxalate solution, in order not to shrink the corpuscles, thereby getting low results.

The amount of dye in the plasma is determined with a Koenig-Martens spectrophotometer.

Injection of brilliant vital red into the vein of a normal human should precede by 6 minutes the taking of a sample, that length of time being required to mix the dye with all of the plasma of the body.

**PNEUMONIA.—ETIOLOGY AND PATHOGENESIS.**—During the past 2 years J. T. Smeall (Brit M J 1:661 (Apr 18) 1931) has typed

over 150 strains of pneumococcus isolated from lesions in different parts of the body. He states that the pneumococcus most commonly found in the eye, nose and accessory sinuses belongs to Group IV. In acute otitis media and mastoiditis, Type III strains and Group IV organisms were found in about equal numbers. The type-specific strains showed a greater tendency to infect the meninges. Attention is drawn to the important part the streptococcus plays in acute middle-ear and mastoid disease. *Streptococcus pyogenes* was found in the majority of cases. The most prevalent type pneumococcus in cases of lobar pneumonia was found to be Type II. In cases of empyema due to pneumococci, the Type I strain was present in a large percentage.

The incidence of pneumococcus types in 186 patients suffering from acute lobar pneumonia in Edinburgh during the past 18 months, J. M. Alston and D. Stewart (Brit. M. J. 2:860 (Nov 22) 1930), is recorded, as well as the mortality rates associated with the different types. Type I was found in 53 cases; Type II in 75 cases; Type III in 7 cases; and Type IV in 47 cases. The death rate in relation to type incidence was: Type I, 23 per cent; Type II, 31 per cent.; Type III, 71 per cent, and Type IV, 10 per cent.

In a study to determine the relative frequency of the several types of pneumococci in the different pneumococci affections (lobar pneumonia, bronchopneumonia, meningitis, peritonitis) in the Philippines, C. Monserrat (J. Philippine Islands M. A. 10:424 (Oct.) 1930) found that in lobar pneumonia the Type IV pneumococcus was frequently observed; next came Type I. Type III was rarely observed, and Type II was not isolated in the 26 cases of

this series. The right lung was more frequently involved, but bilateral lesions seemed to occur more often in Type IV. In bronchopneumonia of children, Type IV also predominated. The incidence of this type followed closely the incidence of the same type in the lobar pneumonia of adults. Empyema was frequently associated with the Type IV pneumococcus in the bronchopneumonia of children. The preponderance of the Type IV pneumococcus in the bronchopneumonia of children in the Philippines agrees with the findings of Penfold, in Australia. The relatively low mortality and morbidity in lobar pneumonia in the Philippines may be explained by the relatively low incidence of the typical types of pneumococcus. In primary pneumococcus meningitis Type IV was also frequently isolated.

A. D. Frazar (Brit. Med. J. 2:140 (July 26) 1930) reports a case of pneumonia and empyema apparently caused by a nonlactose-fermenting *coliform bacillus* possessing special biochemical and agglutinative characteristics. Three specimens of pus aspirated from the pleural cavity on different dates were examined, and a Gram-negative bacillus isolated on each occasion, giving the same biochemical and agglutination reactions. While the organism has, antigenically, as well as biochemically, something in common with the *paratyphosus B bacillus* and the *aertrycke bacillus*, it is distinct from these organisms. The clinical course of the infection bears a striking resemblance to that of many cases of psittacosis. The sudden "influenzal" type of onset, the dry cough, the slow pulse and respiration rate compared with the high temperature, are found in psittacosis, but there is no history in the case of contact with a parrot, and the organism differs from the

strains which used to be considered the cause of psittacosis. The organism is, therefore, closely allied to the *paratyphosus B-aertrycke* group, but differs materially from these organisms in failure to ferment dulcitol and in its specific serologic qualities.

A. D. Fraser (Lancet 1:70 (Jan 11) 1930) states that the occurrence of lung lesions in the acute stages of rheumatic fever has long been recognized, but the pathology has been little investigated, owing to the lack of autopsy material. In 2 cases of acute fatal rheumatic fever the lesion is likened to an acute interstitial pneumonia with a predominance of cell proliferation, edema, and arteritis, with subsequent fibrosis. The opinion that this is associated with the causative agent of rheumatic fever is supported by the finding of typical *Aschoff nodules* in the interlobular septa and other interstitial structures. Not only the lung itself was involved, but the pleura and the bronchial wall, as well as the lining of the epithelium of the air passages. One case showed definite Aschoff nodules in the myocardium, while the other had a patchy fibrosis scattered through the muscle, not localized in nodules.

It has been observed by T. Francis, Jr. and W. S. Tillett (J. Exper. Med. 52:573 (Oct.) 1930) that the majority of patients convalescent from pneumonia due to Types I, II, and III pneumococci develop at the time of recovery circulating antibodies for the homologous type of organisms. At the same time an immediate wheal and erythema reaction followed the intradermal injection of the homologous type-specific polysaccharides in 100 per cent. of Type I patients, 58.8 per cent. of Type II patients, and 44 per cent. of Type III patients. In a group of 18 cases re-

peatedly tested with the type specific polysaccharides, 10 developed in the second or third week of convalescence circulating antibodies for one or more heterologous types. In none of 21 control patients was this phenomenon observed. It is suggested that the development of circulating antibodies for heterologous types of pneumococci was associated with the previous intradermal injections of the type-specific polysaccharides.

**COMPLICATIONS.**—E. de Massary and Y. Boquien (Bull. et mém. Soc. méd. d'Hôp. de Paris 53:1100 (July 22) 1929) report a case of pneumonia with a complication of *multiple cerebral thrombosis* in a patient 27 years of age. He had already passed the crisis and seemed on the way to recovery, when his temperature suddenly rose. Symptoms of diffuse pyramidal irritation were noted. Spinal puncture showed a normal cerebrospinal fluid, which contained no cellular elements and 0.15 grams of albumin. The patient died in the afternoon of the same day. Necropsy showed a typical focus of hepatization at the base of the right lung; the heart and abdominal organs were in perfect condition. In the brain, however, the following changes were noted: The left hemisphere contained a small red focus of softening and showed a blotched aspect of the gray nuclei. In sections of the right hemisphere the perisylvian convolutions were friable and the meninges were adherent to the brain. The white matter was vascularized and hemorrhagic. A large portion of the right middle cerebral artery was thrombosed and microscopic examination showed that it contained a fibrinous clot with many polymorphonuclears; the walls appeared to be intact. According to de Massary and Boquien,

the rapid fatal evolution in this case may have been caused by the extent of the thrombosis, the bilateral involvement, and the double obstruction of the circulation from the venous and arterial thromboses

E Fricks (Am J Surg 8 48 (Jan) 1930) feels that the appallingly high mortality figures of pneumococcus *peritonitis* can be reduced by not operating in the acute diffuse forms but by treating them expectantly. He reports 10 cases—8 children and 2 adults. Six of the children had had whooping cough at some time before their present illnesses. With 1 exception, none of the 8 children had had a cough before the onset of the abdominal pain. The pain started suddenly in all 8 cases. In 1 case there had been a similar mild attack 1 month before. Examination of the lungs revealed signs suggestive of bronchopneumonia in 5 of the cases on the day of admission, which would mean about 1 or 2 days after the actual onset of the illness. Examination in the other 3 cases showed no lung changes. Seven of these patients were operated on the day of admission, and an abdominal puncture was done on the other child the day following admission. The appendix was removed in all the patients operated upon, and in 1 case both the tubes also.

Pneumococci were found in the abdominal pus in all the cases, and all 4 types were represented in the series. In only 1 case was a blood culture and a spinal fluid culture taken, both of which showed pneumococci. Six of the 8 patients died, among them being the child in whom only an abdominal puncture had been done, and also 1 who had received pneumococcus serum. Both the cases in which recovery took place showed a tendency toward chronicity

from the start. One of these cases was a boy, and the other a child who later developed metastatic foci in which pneumococci were demonstrated.

Both the adults were women. One was admitted with a beginning peritonitis following abortion. The blood culture showed pneumococci. She was not operated on, but was treated with pneumococcus serum and survived. The other patient was suddenly seized with abdominal pain 36 hours before admission to the hospital. The lungs did not show any changes. The abdomen showed the picture of generalized peritonitis with tenderness more marked on the right than on the left. A diagnosis of ruptured appendix was made. At operation, free pus coming from a bilateral pyosalpinx was found in the peritoneal cavity. Both tubes and the appendix were removed. Pneumococci were demonstrated in the pus from the right side.

**DIAGNOSIS.**—A method of *microscopic agglutination* is described by A. B. Sabin (J Infect Dis 46 469 (June) 1930), in which the organisms are smeared with the serum on a slide, allowed to dry rapidly, and stained. By this method the type of infecting pneumococcus can be determined in 2 ways: (a) with the patient's sputum, usually within 3 to 4 hours after its injection into the mouse; (b) with several drops of the patient's blood, by determining the type of agglutinins that are neutralized after the administration of polyvalent serum. This procedure is applicable to a limited number of patients; it is especially indicated in cases in which sputum is not obtainable and it is desired to know whether the infecting pneumococcus is of a type for which antiserum is available. The microscopic agglutinin test on a single drop of pa-

tient's blood can be used to demonstrate the presence or absence of active infection, as indicated by the neutralization of homologous agglutinins in the circulation, as well as the active production of antibody, and may thus be used as a guide in controlling the dosage of anti-pneumococcus serum

**PROGNOSIS.**—In discussing the prognostic value of the initial leukocyte and differential count in lobar pneumonia, R P Middleton and J H Gibbon, Jr (Am J M Sc 180:31 (July) 1930) assert that absence of leukocytosis is an unfavorable and leukopenia an ominous sign. A high total leukocyte count, especially 20,000 per c mm or above, is reassuring. Suppression of the total lymphocyte count below the low normal of 1200 per c mm is of bad import, having been noted in more than half of the fatal cases. Among 100 patients who recovered from pneumonia, 68 per cent had negative indexes of resistance at the initial blood count. A negative index of resistance cannot, therefore, be regarded *per se* as alarming. Nevertheless, a low index of resistance is unfavorable. A slight alteration of Walker's formula is suggested with the object of making it express more clearly the idea for which he designed it. The specific nature of the body's response to various types of infection makes caution necessary in drawing prognostic conclusions from differential counts. The initial total leukocyte and differential leukocyte counts are frequently useful in the prognosis of pneumonia. Paradoxical results are sufficiently common, however, to discourage undue dependence on their prognostic significance.

**TREATMENT.**—Interest of clinicians throughout the world is engaged in the specific treatment of pneumonia.

The only impressive findings are limited to patients treated in the first 1 to 3 days of the disease in Type I pneumococcus infections. It is interesting to note that even where an effort is made to have adequate controls, with the exception before stated, the percentage of recoveries in the serum treated cases is not better than the percentage of recoveries used to be in the old days when nursing care and attention to alleviation of symptoms were emphasized, as they deserve to be.

Lord Dawson (Lancet 1 625 (Mar 21) 1931), before giving Felton's serum, tests the patient for hypersensitiveness by instilling 2 drops of undiluted serum into the eye. Within a quarter of an hour the conjunctiva will be injected if the patient is sensitive. A more sensitive intradermal test with 10 per cent of serum in physiologic sodium chloride solution gives a positive reaction in a susceptible patient. The hypodermic use of epinephrin affords protection in the event of anaphylactic reaction appearing. The results of the use of Felton's serum are encouraging, though not yet conclusive. There are grounds for thinking that, besides cutting down the mortality, in Types I and II the prompt use of Felton's serum cuts short the attack. The author suggests that the time has come for a wider trial of Felton's serum, used promptly as soon as pneumonia is diagnosed without waiting for the typing of the strain.

For combating *anoxemia*, oxygen inhalations are given. For routine treatment the nasal catheter (number 10) is the best and is adaptable under all conditions of hospital and home. By using calibrated reducing valves, the amount of oxygen delivered can be determined and regulated. If 2 liters a minute are delivered through the catheter, the in-

spired air contains 30 per cent of oxygen and the latter can be raised to 35 per cent. Masks for oxygen administration are impracticable because they distress the patient. The use of the funnel and tube does not give inspired air a higher oxygen value than 22 per cent and is of little use. When the abdomen is distended and the bases of the lungs are apt to lose functional efficiency, the latter can be improved by a brief inhalation of a mixture of **oxygen** and 5 per cent. of **carbon dioxide**.

Elimination should be promoted and it is interesting to note that solutions of **ammonium acetate** and **potassium citrate**, long established by experience, are being justified by the more exact knowledge of pharmacology. Watching the blood-pressure is a helpful guide. If it falls, and especially the diastolic pressure, **strychnine** is valuable. **Digitalis** is indicated in cardiac insufficiency and auricular fibrillation. The hesitancy to use **opium** in pneumonia is fortunately passing, though in some quarters it still lingers. For *pain* and damping down ineffective *cough*, it is essential. The cough which derives itself from a pneumonic area can do no good; that area is not functioning and should be kept at rest. The fear that opium in medicinal doses will depress the respiratory center is a bogey. On the other hand, the muscles of respiration become exhausted by their constant use in coughing. The only condition under which opium may require to be withheld or used with great restraint is in a generalized bronchitis with an exudate blocking the tubes. When a patient is just restless and sleepless, a hypnotic is better than opium; often a combination is good. In acute infection, **chloral hydrate** and **bromide** still hold an im-

portant place. **Alcohol** has the advantage of being a food that does not require digestion. It lightens worries and helps repose and sleep.

**Serum Therapy.**—The use of **pneumococcus concentrated immune bodies** in pneumococcus Type I and Type II pneumonia is considered by H. S. Baldwin (Am. J. M. Sc. 181:788 (June) 1931) to be relatively free from dangerous reactions and serum sickness, and it makes it possible to give large amounts of antibody in a short space of time. By using these extracts favorable clinical results are often obtained, and it seems to be definitely established that with them pneumococcus Type I and II bacteremia can be eliminated in many cases and a favorable outcome results. Although the best results are obtained when specific therapy is started early, evidence is given to show that as long as the pneumonic infection appears active specific therapy is indicated. The specific therapy of pneumococcus Type II pneumonia, which heretofore has been a discouraging procedure, seems to have definite value when concentrates of high unit value are given in large amounts.

H. Lichtenstein (Med. Klinik 25 1966 (Dec. 20) 1929) employed serum therapy in the treatment of 23 patients with lobar pneumonia. He found that so-called **polyvalent pneumococcus serum**, which was prepared with Types I and II pneumococci, exerted a certain influence in some cases, whereas in others it was not effective. In those cases that were affected by the serum therapy, the temperature decreased, the pulse became more regular and the general condition improved. However, the pneumonia itself was not affected. Animal experiments, as well as the clinical experience of other authorities, indicate



that serum which is prepared with Type I pneumococci should be effective in pneumonia of that type. It was, therefore, surprising that the best results were obtained in pneumonia caused by Type IV pneumococci. From this observation the author concludes that the polyvalent serum is not type specific, but that the reactions are due to the action of the protein bodies. He stresses the point that the nonspecific action of the protein bodies is characteristic only for the polyvalent pneumococcus serum. Monovalent serums had not been employed in these cases.

J. Cowan, R. Cruickshank, D. P. Cuthbertson, J. Fleming, and A. W. Harrington (*Lancet* 2:1387 (Dec 27) 1930) discuss in the first part of their presentation the causes of death in pneumonia, stating that this may result from cardiac failure, anoxemia, intoxication, or complications. It is the intoxication that it is possible to render less severe by the use of the specific serum of Felton. They make it their habit, on the admission of a patient suffering from pneumonia, to give immediately 10,000 units of Type I and II intravenously, following this, as a rule, every 8 hours with a similar dose until the temperature falls below 102° F (38.9° C.). In the meantime, the sputum is typed and if not of the Type I or II group, apparently the serum is stopped. Of the 58 patients reported upon, 41 cases were of Type I and II, with a mortality rate of 7.3 per cent. In the other cases the mortality rate was 28.4 per cent. As controls, they used the death rates which appeared between 1906 and 1929—not a very satisfactory control, incidentally.

Physicians of the Royal Infirmary of Edinburgh (*Lancet* 2:1390 (Dec 27) 1930) report a somewhat larger series

of cases, more adequately controlled, as the patients as they came in were segregated—1 for control, 1 for serum treatment. Of the serum-treated Type I individuals there were no deaths, while there were 5 in the control group. In the Type II pneumonias there were 5 deaths and 10 deaths in the control series. They state that in a disease such as pneumonia, a small series of cases is not a sufficient number upon which to base reliable statistics. Furthermore, they call attention to the fact that the death rate of the control cases undoubtedly was higher than in the serum-treated cases because of the fact that the controls happened to be considerably older than the treated patients. The serum, however, seemed to lessen the severity of the disease and shortens the febrile period. Anaphylactic phenomena were observed in only 2 patients. Both of these 2 reports are highly suggestive, at least, of the value of Felton's serum.

A series of 239 cases of Type I pneumonia treated with Felton's serum are reported by R. L. Cecil and Norman Plummer (*J. A. M. A.* 95:1547 (Nov 22) 1930), showing a death rate of 20 per cent. as compared with a mortality rate of 31 per cent in a control series of 234 untreated cases. There is a further reduction in death rate to 11.7 per cent in cases treated within 72 hours after onset. The authors further state that Type I serum is no longer in the experimental stage and when administered early and in adequate dosage, the clinical results are striking. The present study demonstrates that concentrated serum possesses all the therapeutic value of the unconcentrated preparation. Furthermore, concentrated serum has a much higher potency and a lower content of chill-producing substances and horse serum proteins, which

make it more easily administered and less frequently followed by chills, serum reactions, and serum sickness

The value of injecting **homologous convalescent serum** in the treatment of lobar pneumonia has been investigated by R T Beebe and W D Sutliff (New England J Med 203 823 (Oct 23) 1930) To obtain the best results treatment must be started early, using larger quantities of a serum having a high protective power for mice against the homologous organism Blood from selected patients was collected 4 to 7 days following the crisis, since protection has been shown to be at its maximum at that time The donors were those in whom the disease had run a typical course, and in whom the type of organism had been definitely determined From 300 to 500 cc of blood was collected into a closed flask and allowed to clot at room temperature for 6 hours. The serum was then placed in an ice-box for 24 hours, pipetted off, passed through a Berkefeld filter, pipetted into flasks, and stored in an ice-box The serum was shown to contain a certain amount of specific protective substance for mice Two patients with Type II and 1 with Type III lobar pneumonia were given intravenously amounts varying from 310 to 440 cc within 48 hours on the third and fourth days of the disease One of the Type II patients made a normal recovery after running the usual 8 days' course, while the other 2 became progressively worse and died Although treated under favorable circumstances, the authors conclude that the results fail to show any benefit from the use of homologous convalescent serum

Schottmuller (Deut. med Wchnschr. 56.863 (May 23) 1930) points out that in a considerable percentage of

cases of lobar pneumonia the fever abates gradually on the sixth or seventh day or at the beginning of the second week Simultaneously, the general condition improves considerably, in spite of the fact that the pathologic process still persists for a considerable time and that the pneumococci are still found in the sputum These observations indicate that certain immunity processes determine the favorable outcome and from this the author concludes that **serotherapy** might be helpful He used serum from convalescents whose pneumonia had been caused by the same type of pneumococcus as that of the patient The serotherapy did not show marked effects However, it should be considered that it was not possible to employ it during the first days of the disease The author recommends that this form of serotherapy of lobar pneumonia be further investigated, especially in larger hospitals He states not only that **convalescent serum** should be extracted and properly stored but also that **blood transfusions** (up to 1 liter) should be made directly from the **convalescent to the patient**. It is, of course, necessary that the blood groups be identical The author points out that this form of serotherapy has the advantage that it avoids serum sickness, a condition that frequently develops when animal serums are employed However, additional investigations will be necessary to prove whether the treatment with convalescent serum is of value.

**Miscellaneous Methods.**—A A Lilien (Arch. Physical Therapy 11:155 (Apr) 1930) feels that **diathermy** is valuable in the treatment of pneumonia Its effects are due to the physical action of heat on the metabolic processes as well as on the action of the enzymes. But, he says, diathermy is not the only

therapeutic agent to rely on. General medical care is always of high importance. Diathermy, with proper technic, is indicated in all forms of pneumonia except in aspiration pneumonia, and in pneumonic complications (closed empyema, pulmonary abscess and decompensated heart). Diathermy treatment has proved a good prophylaxis against complications and appears to be of value in treating some of the postpneumonic complications (unresolved pneumonia, asthmatic bronchitis, and chronic bronchitis).

Most cases of pneumonia when treated by diathermy show marked improvement in the respiration, pulse rate and character, cyanosis, and general feeling of the patient, according to H. E. Stewart (Brit J Actinotherapy 4:238 (Feb.) 1930). The drop in temperature by lysis, which occurs in more than 96 per cent of all treated cases, seems to indicate clearly that diathermy modifies the usual course of this disease. No other measure, medicinal or otherwise, indicated by the patient's condition, need be set aside because of the use of diathermy. In the giving of approximately 8000 treatments for this disease, not a single accident or untoward effect has occurred. It is, therefore, more safe than many medical and surgical procedures used as a routine. There is considerable evidence at hand that the mortality in pneumonia may be reduced one-half or more, particularly when treatment is instituted early.

It is pointed out by B. Scholz (Deutsche med Wchnschr 56:1555 (Sept 12) 1930) that in many instances hypertension can be counteracted by reducing the sodium chloride content of the food. This indicates that sodium chloride influences the circulation, and it has been found that its administration effects a

stimulation of the vasomotor nerves. In pneumonia, the focus of infection absorbs large quantities of salt, and in the other organs of the body a sodium chloride deficiency develops. It is probable that this lack of sodium chloride is the cause of the vasomotor weakness. In order to stimulate the circulation during pneumonia, it is, therefore, advisable to supply the organism with sodium chloride. *Care should be taken that the diet is not lacking in salt.* In addition to this, about 10 Gm ( $2\frac{1}{2}$  drams) of **sodium chloride** should be given daily. However, because some patients have an aversion to salt it should be administered in the form of **sodium chloride injections**. The author recommends intravenous injection of 100 Gm ( $3\frac{1}{3}$  ounces) of a 25 per cent solution. In order to avoid tachycardia, the injection should be given slowly. In patients with a weak heart, however, sodium chloride injection is contraindicated. In patients with severe congestion in the pulmonary circulation it is advisable to precede the injection with a venesection. If these precautions are taken complications do not develop, and the stimulation of the circulation, which follows the injection, often has a life-saving influence.

The use of dextrose in pneumonia has been favorably reported upon by W. W. G. MacLachlan, G. J. Kastlin and R. Lynch (Am J M Sc 179:93 (Jan.) 1930). From 400 to 600 Gm. ( $13\frac{1}{3}$  to 20 ounces) of dextrose is given by mouth daily. The most practical method of accomplishing this is to dissolve 200 Gm. ( $6\frac{2}{3}$  ounces) of dextrose in 1000 cc (1 quart) of water, to which is added the juice of 2 or 3 lemons.

J. Brodie (Canad. M. A. J 21:541 (Nov.) 1929) states that it is generally agreed that failure of some part of the

circulatory system is an important factor, often leading to a fatal outcome, in many cases of pneumonia. The mechanism of the failure of the circulation is not well understood, since pneumonia produces no definite anatomical changes in the heart, as do some other infectious fevers. There are certain factors in this disease that must throw an extra burden on the heart, among these are impairment of the pulmonary circulation, disturbance of respiratory function which causes anoxemia, and toxemia. The strain on the right heart resulting from impairment of the pulmonary circulation, the widespread pernicious effect of anoxemia on the whole cardiovascular system, and the weakening of the peripheral circulation caused by the toxemia, not to mention other factors, all affect the circulatory apparatus in so many vital points that it often becomes exhausted, and finally breaks down. In treating pneumonia, complete physical and mental rest is of supreme importance, and to obtain this the administration of an opiate or morphine is often wise when signs of excessive secretion in the air passages are absent. Opiates should be replaced by milder sedatives after the fourth day of the disease. *Digitalis* may be given as a routine measure in all cases of pneumonia. In order to avoid overdigitalization, 40 to 60 minims (2.6 to 4.0 c.c.) of the tincture, or a corresponding dose of the powdered leaf, should be given daily until the fifth day, when the amount is reduced to 30 minims (2.0 c.c.) daily, watch being kept for the usual toxic effects of the drug. The effective administration of oxygen in adequate dosage is supportive, and tends to prolong life until the mechanism of immunity is able to accomplish recovery. Six of the so-called cardiac stimu-

lants are discussed. Alcohol is only a sedative, and may be of value as such; the administration of large, repeated doses may do harm by hampering the production of immunity. Strychnine is unsatisfactory, both as a cardiac and as a respiratory stimulant. Adrenalin is useful when the blood-pressure falls and the heart sounds grow feeble; its use needs caution, and small repeated doses are safer than a single large one. Pituitrin is also useful, but less so than adrenalin. The efficacy of caffeine is doubtful. There is no proof that camphor acts on the heart muscle, although it appears to exert some reflex on the medullary centers.

The suggestion that irradiation should be instituted in all cases of pneumonia showing definite x-ray signs of delayed resolution 3 weeks after the onset, is made by E. A. Merritt and E. M. McPeak (*Am. J. Roentgenol.* 23:45 (Jan.) 1930). Of 7 cases thus treated by the authors, 4 cleared up entirely, 2 improved definitely, and 1 was unchanged.

## PNEUMONIA IN CHILDREN.

—ETIOLOGY.—A classification of pneumonia as it occurs in infants or nurslings is given by P. Heim (*Monatsschr f. Kinderh.* 45:119 (Oct.) 1929) as follows:

1 Lobar pneumonia, uncommon in this age group and usually caused by Type IV pneumococcus.

2 Secondary pneumonia. (a) Aspiration, chiefly of the newborn; (b) associated with severe nutritional disturbance, probably as a result of circulatory weakness; (c) following acute infectious diseases as measles and pertussis; (d) septic, may result in abscess or empyema; (e) catarrhal or bronchopneumonia, (f) tuberculous.

J. D. Trask, C. O'Donovan, Jr., D. M. Moore and A. R. Beebe (J. Clin. Investigation 8:623 (June) 1930) have made a comparative study of pneumonia due to fixed types of pneumococci in adults and children in identical periods of time and in a given locality (New Haven).

Fixed types of pneumococci were responsible for most of the cases of lobar pneumonia in both children and adults and were found infrequently in cases of bronchopneumonia. The mortality in those cases caused by Types I, II, II atypical, and III, was approximately  $4\frac{1}{2}$  times greater in adults than in children, 10 per cent in 73 cases in children, and 43 per cent in 90 cases in adults. Particularly is this difference noted in cases of lobar pneumonia caused by Type III pneumococcus. Of 10 cases in children all recovered.

It is of considerable interest that blood stream invasion was both less frequent and less intense in children than in adults. Protective bodies were found to appear in the urine of children, as in adults, about the time of recovery. Type specific agglutinins also were found in children, but less frequently than in adults, and apparently less frequently in younger than in older children.

The authors argue that there must be some essential difference in the reactivity of children and adults to pneumococcic infection. To quote them: "In explanation it may be suggested either that children possess a mechanism of defense different (in a positive sense) from that of adults and perhaps analogous to the defense of the rabbit against pneumococcus Type III described by Tillet, or that adults acquire a susceptibility to pneumococcus substance, which then could act against the defense

mechanism by which heavy blood stream invasion is prevented."

The majority of pneumococcus infections in children fall into the unclassified Group IV. It is well known that there are a number of different strains in this group. From a standpoint of prognosis and specific treatment, it would seem desirable to identify the individual members.

N. Plummer, A. Rain and S. Shultz (Am. J. Dis. Child. 40:557 (Sept.) 1930) have made a bacteriologic study of pneumonia in children with particular attention applied to the identification of these previously unclassified members of Group IV into the 10 types (Group IV to XIII), as described by G. Cooper, M. Edwards and C. Rosenstein (J. Exper. Med. 49:461 (Mar.) 1929). By the old grouping, 81.6 per cent. of these cases fell into Group IV, whereas by this new classification, only 49.7 per cent. remained unclassified. Type VI was found more frequently than Type I, and Types IV, V, VI, VII, and IX occurred more often than either Type II or Type III.

They also checked the accuracy of the swab method for collecting infected material. In 37 of the 147 cases they obtained cultures from the sputum, blood, ear exudate or chest fluid, or from specimens procured by post-mortem puncture of the lung or at autopsy. In 31 or 84 per cent. the same organisms were found by one or more of the above methods as by the swab method.

An effort to determine the type of organism causing pneumonia in infancy was made by R. Neumann and H. Happe (Monatschr. f. Kinderh. 45:141 (Oct.) 1929). They did lung punctures in 46 cases and found organisms in 21 of them. Pneumococci were found in 9 instances, all of which belonged to

Type I, staphylococci in 8, 2 of which were hemolytic, and streptococci in 4, 3 of which were hemolytic

J B Ellison (Arch Dis Childhood 6 37 (Feb) 1931) has demonstrated microorganisms of the influenza group in 46 per cent of a series of 75 cases of pneumonia complicating measles. He is of the opinion that the pneumonia which is associated with measles is frequently of the acute interstitial type, and that it is a frequent precursor of chronic nontuberculous pulmonary disease. The *Bacillus influenzae* is accorded credit as the chief etiologic factor.

M. C. Schroder and G. Cooper (J Infect Dis, 46:384 (May) 1930) report an epidemic of pneumonia, bronchitis, and common colds in a children's home. The more interesting observations were (1) the explosive nature of the epidemic and the short space of time in which it reached its height, 55 patients being admitted to the hospital on the seventh day after the first patients were admitted, (2) the extreme infectivity of the organism, (3) the prostration and cyanosis which accompanied the apparently milder cases, and (4) the definite isolation of an infecting organism commonly classified as belonging to Group IV of the pneumococcus group, but which in the research laboratory has been definitely determined as a member of Type V.

**DIAGNOSIS.**—E. Cassouts, R. Poinso and E. Zuccoli (Arch de méd d enf 33 546 (Sept) 1930) are convinced that pneumonia occurs in nurslings. Typical cases present the same symptoms that accompany pneumonia in older patients. Although the helmet-shaped shadow revealed by x-ray examination is present also in chronic syphilitic pneumopathies, tuberculous pneumonia and pseudolobar bronchopneu-

monia, the syndrome and development of these diseases is so different that they can easily be distinguished from the typical forms of pneumonia. However, certain atypical or prolonged forms of pneumonia, in which the evolution of the disease is longer and the symptoms more irregular, are difficult to distinguish from pseudolobar bronchopneumonia or splenopneumonia, although their resemblance to the typical forms is marked.

**PROGNOSIS.**—H. P. Jameson (Arch Dis Childhood 4 365 (Dec) 1929) suggests that emphasis is to be placed on the amount, duration, and recurrence of the interstitial inflammation in estimating the *remote* prognosis of pneumonia. Second or third attacks and the occurrence or persistence of upper respiratory infections are particularly liable to cripple a child who has once suffered from this disease.

A very high or a very low leukocyte count has for some time been commonly associated with a low resistive reaction and a consequent high mortality in those infectious diseases which ordinarily react with a moderately high degree of leukocytosis. Confirmatory data that such is frequently the case in the pneumonias of children is recorded by H. F. Meyer (Am J. M. Sc 181 245 (Feb) 1931). Daily white cell counts were done on 100 children with lobar or bronchopneumonia. There were 30 deaths in this series. They found that the mortality was inversely proportional to the leukocyte count, except in children having over 50,000 cells per c mm. Fifteen of those children who died had a count of less than 10,000 cells per c mm, while only 3 recovered. Twenty of the fatal cases had a count of less than 15,000, and there was a tendency towards a steady decrease in the daily



cell counts Of 10 fatal cases with leukocyte counts exceeding 15,000 cells per c mm, 3 exceeded 50,000 Of significance is the fact that all patients with leukocyte count in excess of 50,000 cells per c mm died

They also present evidence to show that suppurative complications and extension of the pneumonia may be anticipated by the sudden increase of the leukocyte count

**PROPHYLAXIS.**—Vaccination against pneumonia is not a generally accredited procedure, for which reason it would seem worth while mentioning the study of Neumann and Happe (*loc cit*) on a group of hospitalized infants A strain of pneumococcus Type I was obtained by lung puncture from an infant with bronchopneumonia Three injections were made at intervals of 7 days Of 128 infants who were vaccinated, pneumonia developed in 8, or 6.2 per cent As a control group they had 322 infants, also hospitalized, who were not vaccinated Of these, pneumonia developed in 34 or 10.5 per cent

**TREATMENT.**—R P Forbes and C L Steinberg (Arch Pediat 48:238 (Apr) 1931) have employed a **mixed respiratory vaccine** in the treatment of 50 cases of pneumonia in children They used as a control group, 66 children who received no vaccine In the vaccinated group the mortality was 18.7 per cent, in contrast to 27.3 per cent in the control group. If the vaccine therapy was started within 48 hours of the onset of the pneumonia, the mortality was only 4.6 per cent., as against 20.6 per cent in the control series

*Abdominal distention* is one of the more disturbing complications of pneumonia in children H P Fine (M J and Rec 131:25 (Jan. 1) 1930) divides it into 2 types, *i e*, (1) that which oc-

curs early in the course of the pneumonia, usually due to some gastrointestinal disturbance, and controlled by relatively simple means, and (2) the type that occurs midway or late in the disease, frequently resisting all therapeutic efforts and considered a bad prognostic sign This late distention, he suggests, may be due to the toxicity of the disease producing intestinal paresis or to circulatory failure

As means of *prevention*, the author suggests a change in all infants with pneumonia from sweet to **acid-milk mixtures**, except in the case of breast-fed infants He prefers the **cultured buttermilks**. Fluids should be forced in order to help combat the toxemia Good nursing care is essential, and the nurse should be instructed to report to the doctor the first evidence of abdominal distention

In *treatment* he advocates most of the usual methods such as **laxatives**, **local warmth to the abdomen**, **colonic irrigations** and **enemas**, **rectal tube**, **hot abdominal packs** and **stupes** and **carmenatives by mouth**. In persistent cases he uses **pituiratin** and **eserine sulphate**.

T M Montford (Brit. M J. 2:757 (Nov 2) 1929) treated 179 cases of acute pneumonia with relatively large doses of oxygen injected into the subcutaneous tissues The value of oxygen employed in this way has been much discussed He found that the mortality of the disease is unaffected The average length of the febrile stage is shorter and the average length of the course of the disease is lessened, especially in bronchopneumonia. The pathological processes are apparently expedited, possibly the stages of hepatization are hastened by an early formation of hydrogen peroxide in the pulmonary tissues

**PNEUMOTHORAX, ARTIFICIAL.** See TUBERCULOSIS, PULMONARY SURGICAL TREATMENT.

**POLIOMYELITIS.—IMMUNITY.**—R W Fairbrother and W. G S Brown (Lancet 2 895 (Oct 25) 1930) examined the serum of various students 6 months after an attack of poliomyelitis had stricken several members of the school. The serums included specimens from convalescent and abortive cases, close and remote contacts. These investigators noted that immunity to the poliomyelitis virus, as shown by the presence of antiviral bodies in the serum, is frequently present in normal people who have been in contact with definite cases of the disease without developing it. The immunity of adults to poliomyelitis is accepted as being due to subclinical affections. This supports Aycock's view.

**PROGNOSIS.**—Under optimal conditions, R H Riley (J A. M A 94: 550 (Feb 22) 1930) was able to obtain from 70 to 80 per cent good recovery, as compared with 20 per cent in cases receiving less intensive therapy. He believes that appropriate treatment should prevent 90 per cent of the deformities which follow epidemics. This presupposes early treatment of the disease, along with the use of human serum, early hospitalization, and the guidance of an orthopedic surgeon as factors of importance which produce low mortality rate, low average of total paralysis, a striking reduction of paralysis of severe grade and complete prevention of deformities.

**PROPHYLAXIS.**—It is pointed out by E Moro (Klin. Wchnschr 9: 2383 (Dec 20) 1930) that the serum of convalescents has virucidal powers toward acute anterior poliomyelitis and

also that the blood of the majority of adults possesses this same power. This is due principally to the presence of specific antibodies. However, therapeutically, the injection of blood from convalescents or from adults has not been effective, due to the fact that the injection is generally given too late. This would indicate, therefore, that injections should be given during the preparalytic stage. However, Moro advocates the injection of convalescent serum for prophylactic purposes and hopes to prevent epidemics in this way. He advises that children under 5 years of age be given an injection of 20 c.c. (5 drams) of fresh blood from one of their parents, and believes that this procedure would give protection for a period of 4 weeks. When indicated, the injection would have to be repeated at the end of that month. In large cities, most of the adults over 50 years of age have specific protective substances in their blood, and injections from one adult usually gives sufficient protection. In the rural districts, however, only about 50 per cent. of adults possess specific antibodies, and here it would be essential to inject mixed blood from both parents, or serum from adults living in the city.

Riley (*loc cit*) considers that no untoward effects from the use of convalescent serum need be feared, and even with an error in diagnosis, no harm will follow from its administration. He thinks that early and repeated spinal drainage and the use of convalescent serum are most important in the preparalytic stage of the disease. It is obvious that to prevent paralysis, therapy should be directed toward the process acting in the central nervous system. Prolonged rest in the recumbent posture is essential. Diagnosis before the stage of paralysis appears is extremely

important, according to Riley. When a patient, especially a child, appears prostrated out of proportion to the temperature, with flushed face, anxious expression, mild injection of the throat, rapid pulse, a coarse tremor or movement, the head tilted on the neck, stiffness of the spine and pain on anterior flexion, with an increase in the cellular and globulin contents of the spinal fluid, the diagnosis of poliomyelitis is definite and convalescent serum should be given.

**TREATMENT.**—H. Eckhardt (Deutsche med. Wchnschr. 57:101 (Jan. 16) 1931) discusses the favorable results obtained in treating cases of acute poliomyelitis during the 1929 epidemic which occurred in Ontario. Early diagnosis and prompt administration of convalescent serum were the outstanding features. Early diagnosis is especially difficult in sporadic cases. The paralytic symptoms are observed between the second and fifth day, but during the preparalytic stage, fever, fatigue and a feeling of weakness in certain groups of muscles are noted. In the majority of cases meningeal symptoms develop, such as stiffness of the neck, aversion to moving the vertebral column, hyperesthesia and a tendency to profuse perspiration.

During the Ontario epidemic, when convalescent serum was given during the preparalytic stage, a quick recovery resulted in more than 80 per cent. of the cases, and the patients who received the serum in the first stage all recovered completely.

This report also shows that arrangements should be made to have convalescent serum on hand when an epidemic develops. Since cases of acute poliomyelitis are especially numerous from July to October, this investigator suggests that, during the summer months,

depots for convalescent serum should be established in various parts of the country. The serum should be obtained from patients who have had an attack of acute poliomyelitis during the last 5 years.

A. Lichtenstein (Ztschr. f. Kinderh. 51:39 (May 18) 1931) reviews his own experiences with treatment during the acute stage. **Mixed serum** from 3 donors was administered intravenously and intramuscularly. For each injection 10 to 20 c.c. (2½ to 5 drams) were used. Occasionally the injections were repeated once in the same manner. The results obtained by the author are not encouraging. In 69 patients treated during the paralytic stage, the mortality was 21 per cent., which is about the same as when convalescent serum is not administered. Of the 38 patients treated during the preparalytic stage, paralytic symptoms developed in 15 and in 8 cases they persisted. One of these patients died of respiratory paralysis and the others recovered with or without paralysis. Twenty of the patients who were given no serotherapy showed the same course of the disease. When convalescent serum is given during the preparalytic stage, however, there is a possibility of a favorable influence, as shown by the action of the convalescent serum in experimental poliomyelitis of apes. In order to be effective, however, it should be given during the first hours or days. This necessitates early diagnosis made possible by early lumbar puncture.

Since in many cases improvement or cure may be spontaneous, L. Delherm (J. de radiol. et d'électrol. 15:321 (July) 1931) believes that the various suggestions offered should be accepted with reservations. This observer states that x-ray therapy is a reasonable treat-

ment at the beginning of the disease or when there is no destruction. Ascending or posteroanterior **electrotherapy**, as well as **diathermy** and **ionization**, may be used with equal effectiveness. These methods assist in cellular exchange when there has been no destruction with sclerotic tissue formation. In the treatment of disturbances due to malnutrition and defective circulation, the limbs or members are to be treated and not the muscles. **Hot baths**, locally, a sort of double-walled boot filled with warm water, **sun baths**, **infra-red baths**, **voltaic current** and **diathermy** are recommended. In the excitomotor treatment of the muscles, the author recommends the **galvanic current** of alternating long wave lengths with the action selective on the degenerating muscles. Even in those muscles showing a reaction of degeneration, but with conservation of excitability, an electric current interrupted with a metronome can be applied, and some time later the faradic current applied in spaced or rhythmic tetanizing shocks, according to the resistance in the muscles that react to the faradic current. **Ultraviolet rays** are said to influence muscular tonicity. As a rule, Delherm uses the 2 currents with a diathermy voltaic combinator, utilizing their double trophic action as well as generating excitomotor current during the passage of the diathermy current.

The later the disease is diagnosed, the more apparent is the pathological process, and many times the clinical findings show advanced paralysis of various muscle groups, not infrequently involving the respiratory function. A small percentage of all cases may require the use of the **Drinker respirator** to save life. This, however, is an expensive and time-consuming procedure. J. L. Wil-

son (New England J. M. 205 597 (Sept 17) 1931) points out that poliomyelitis can prevent efficient respiration in 3 different ways: (1) Directly, by actual paralysis of the primary respiratory muscles—the intercostals and the diaphragm, (2) directly, by disturbance of the nerve centers in the medulla or bulb which controls respiration, (3) indirectly, in patients with paralysis of the pharynx, by the collection of mucus or vomitus around the glottis, causing either by actual obstruction or by setting up irritative spasms of the glottis, constantly interrupted inspiration and consequently shallow, irregular and ineffective respiratory movements.

In the first situation, the lesion exists in the dorsal and cervical cord, and is not, therefore, bulbar, even though respiratory failure does exist. In the second and third conditions, however, involvement of the respiratory center or paralysis of the pharynx is "bulbar."

The respiratory difficulty may be due to 1 or all 3 of these factors or to any combination. The use of the Drinker respirator has been most effective in patients with paralysis of the intercostal muscles or the diaphragm. An attempt to prolong the life of patients with paralysis of the respiratory muscles is sensible only in the hope that much of the paralysis seen in the acute state will be temporary. Time permits a variable return of power to the respiratory muscles. It would appear that some patients with paralysis of the respiratory muscles will regain sufficient muscle power to breathe unaided, provided they can be kept alive by the respirator and free from pneumonia for that period.

In the individual patient showing bulbar poliomyelitis without paralysis of the intercostals or the diaphragm, it is frequently difficult to untangle the cause

of the respiratory difficulty. These patients, however, very rarely can be helped in any way by the apparatus.

The greatest danger incident to using the respirator lies in the difficulty of caring for the patient as a whole. In the last analysis, the survival of a patient with paralysis of the respiratory muscles may depend just as much on proper medical care as on the mechanical efficiency of the respirator, and the patient's position in the machine must be regularly changed. Hypostatic pneumonia is always to be feared. When in doubt, it seems justifiable to offer such patients a therapeutic trial in the respirator.

**PREGNANCY.—COMPLICATIONS.**—P. A. Daly and S. Strouse (J. A. M. A. 96:1655 (May 16) 1931) present their experiences for the past 10 years, in the Chicago Lying-In Hospital, where all obstetric cases that presented any medical complication were examined.

**Diabetes and Glycosuria.**—Fear of the dangers of diabetes in pregnancy or unrecognized benign glycosurias of the renal type have been overemphasized, with consequent overtreatment of the patient, resulting disastrously. Three types of glycosuria are commonly seen in pregnancy, *ie.*, the renal glycosuria, the mild diabetes sometimes developing only during pregnancy, and the severe diabetes.

Patients with renal glycosuria are rendered sugar free only with great difficulty, whereas persistence in a low carbohydrate diet produces acidosis which endangers the lives of mother and child. Patients with a mild but true diabetes developing during pregnancy require only moderate reduction of carbohydrate intake. Patients with severe diabetes can be carried safely

through delivery by the use of painstaking diabetic therapy, especially insulin, but it should be realized that there are inherent dangers and difficulties.

**Heart Disease.**—The pregnant patient with heart disease requires the same therapy as does the normal woman, except for the extra mechanical burden of pregnancy. In a series of 354 patients, 255 (72 per cent) had mitral lesions, 47 (13.2 per cent) had myocardial changes, 24 (6.8 per cent) had combined aortic and mitral disease, 20 (5.6 per cent) had aortic lesions, and 7 (2 per cent) had congenital lesions. Of an entire series of 500, 12 (2.4 per cent) of the patients died.

The object of *treatment* is to maintain or increase the cardiac reserve. This is obtained by **proper balancing of rest and work**. Over-treatment is to be avoided as, for example, insistence on too much rest in bed. W. D. Reid has recently pointed out that the average life of women with heart disease is about the same, whether they have been pregnant or not. Hearts decompensated when labor occurs offer a grave prognosis. When early delivery is desired or subsequent pregnancies are deemed unwise, **Cesarean section** is the best plan. Induction of labor even at term, seems to increase the risk.

**Thyroid.**—It has frequently been suggested that disturbances of thyroid function may be a factor in the production of some of the toxemias of pregnancy. The present status of scientific knowledge of the thyroid is, however, confused. Pregnancy causes both anatomical and functional changes in the thyroid gland. In a small group a syndrome of nervousness, tachycardia and increased blood-pressure indicate a mild *hyperthyroidism* which responds to **iodine** in a few days.

Real *toxic goiter* may occasionally develop in previously normal thyroids. Pregnancy beginning during hyperthyroidism and continuing is, however, rare. Patients with hypothyroidism are subject to edema, albuminuria, hypertension, and eclampsia. These symptoms may promptly disappear when sufficient thyroid is given to increase or maintain the metabolism at the higher level.

**Treatment**—The pregnant state demands increased secretion of the thyroid gland. If the gland is normal and the supply of iodine in the body is adequate, this increase of thyroid secretion will be sufficient. Twenty-nine cases of *exophthalmic goiter* and 12 of *adenomatous goiter with hyperthyroidism* which were associated with pregnancy, were observed by R. D. Mussey and Wm. A. Plummer (J. A. M. A. 97: 602 (Aug. 29) 1931) in the Mayo Clinic between January, 1923, and January, 1930. The onset of symptoms occurred during pregnancy in 4 of the 29 cases.

Evidence indicates that hyperthyroidism resulting from *adenomatous goiter* is not satisfactorily controlled by iodine and that it is safer to remove the adenomatous tissue if this condition is present.

The use of compound solution of iodine in doses of 10 drops 3 times a day, in cases of *exophthalmic goiter* should be followed by distinct improvement and definitely lowered basal metabolism within 2 weeks. Recrudescence of the disease often occurs in spite of the continued use of iodine. Except in certain cases in the last months of pregnancy, partial **thyroidectomy** should be performed without delay if the *exophthalmic goiter* does not show complete or nearly complete remission

within 2 weeks after the institution of treatment with iodine, as delay may cause permanent damage.

When the strength of the patient is diminished as a result of the severity of the hyperthyroidism, it may be necessary to shorten labor by **forceps** or **version** or rarely by **Cesarean section**.

G. S. Fahrni (Canad. M. A. J. 23: 645 (Nov.) 1930) claims that a patient having *hyperthyroidism* who is less than 5 months pregnant should have a **thyroidectomy** as this is without danger. In women from 6 to 9 months pregnant, Fahrni favors **conservative treatment**. In considering the advice to give women who have recently had a thyroidectomy, Fahrni advocates advising them against pregnancy for at least 2 years, but should they become pregnant in the interval, the gestation does not necessarily have to be interrupted.

**Syphilis**.—J. R. McCord, discussing this subject before the Philadelphia County Medical Society, May 13, 1931, claimed that the incidence of syphilis and pregnancy in the United States is about 10 per cent; it is much higher in negro women. During the past 7 years the incidence of positive Wassermann reaction in the Clinic of the Department of Obstetrics of Emory University School of Medicine has been around 20 per cent.

The consensus of opinion is that syphilis does not cause early abortions. McCord is inclined to believe that this is not true, as he found the organisms of syphilis in a fetus which weighed 25 Gm. and was 10 cm in length and again in a 40 Gm fetus which was 14 cm in length. This at least indicates that there are many early ovular infections.

The microscopic examination of a placenta for syphilis is unreliable. Although there is no distinctive histologic



picture of syphilis of the placenta, the microscopic field of a mature or near mature syphilitic placenta, with its large, crowded villi, the increase of connective tissue, and the almost complete loss of vascularity, occurs often enough to be of distinct diagnostic aid. Such a picture can practically always be checked by positive bone changes or the presence of the *Treponema pallidum* in the baby. A positive diagnosis should not be made upon restricted areas of such histology, but should cause suspicion and a careful follow-up should be made of the babies.

The histologic diagnosis of syphilis in a premature placenta is exceedingly difficult and requires confirmatory evidence which, fortunately, is usually present.

Of all dead syphilitic babies whose bones were examined by the x-ray, 50 per cent were positive. The detection of syphilis in the baby by the x-ray alone, gives a positive incidence that is about 15 per cent. higher than the positive incidence obtained by finding the organisms in the stained tissues.

**Toxemias of Pregnancy.**—H J Stander and J. F. Cadden (Bull. Johns Hopkins Hosp 47:382 (Dec) 1930) do not find an increase of acetone bodies in the blood in normal pregnancy, although both uncorrected and corrected acetone values are above the average for normal nonpregnant women. In the toxemias of pregnancy, however, as well as the low reserve kidney and nephritis complicating pregnancy, there is a tendency toward an accumulation of acetone bodies in the blood, while in eclampsia there is a definite hyperacetonemia which probably helps in the production of the uncompensated alkali deficit so often seen immediately after a convulsion.

It appears that a disturbance in the oxidation of fatty acids occurs more readily in pregnant women with the production of ketone substances. This may, in part, explain the lowered alkali reserve in the blood of pregnant women. A decrease in maternal carbohydrate, resulting from a drain on it by the fetus, or a change in the maternal fat metabolism, may be the cause of the ketosis. Decreasing fat and increasing carbohydrates is, therefore, indicated in the diet of pregnant women.

**Differential Diagnosis.**—C H Peckham and M L Stout (Bull. Johns Hopkins Hosp 49 225 (Oct.) 1931) reexamined two-thirds of a series of 545 consecutive toxemic patients (excluding vomiting and eclampsia) from 4 months to 4 years after delivery and at that time 40 per cent. of them were found to have a definite chronic nephritis. The differential diagnosis between nephritic and nonnephritic toxemia frequently cannot be made during pregnancy or the puerperium, and even at 6 weeks after delivery the diagnosis is sometimes incorrect. Nephritis is seen more frequently in the older age groups and among multiparas. Two-thirds of the non-nephritic toxemias occur in women under 25, and a similar proportion are primiparas. A marked hypertension (systolic 200 mm or more and diastolic 150 mm or over) is more frequently associated with nephritis, although an occasional case of pre-eclampsia is seen with this reading. Albuminuria and its amount is not of prognostic import. The presence or absence of casts in the urine likewise does not give differential information. The phenolsulphonphthalein and Mosenthal renal function tests give almost identical results in the 2 types of cases. Edema occurs in the same proportion of cases

in the 2 groups. Toxemia patients in general seem to have shorter and easier labors than normal, however, the fetal mortality is high, particularly in nephritis. The blood-pressure is higher on discharge in the nephritic type. However, many women who have nephritis leave the hospital with a normal blood-pressure, while about a fifth of the women later returning normal, still have hypertension. Albuminuria on discharge is noted in relatively the same proportion of cases, nephritic or non-nephritic. Even 6 weeks after delivery, many normal women still have hypertension and albuminuria; while a small number of nephritic patients appear normal in these respects. Only 7 per cent of non-nephritic patients show hypertension or albuminuria prior to the seventh month. This would seem to indicate that chronic renal damage may be a result of the toxemic process. If vomiting and eclampsia are excluded, 1 of every 3 women seen with a toxemia of pregnancy will ultimately be found to have nephritis. Except in perfectly obvious cases, it seems better to defer the final diagnosis until 4 months after delivery, although a diagnosis intelligently made at the time of discharge from the hospital is incorrect in only 1 case in 9.

**DIAGNOSIS.**—At the scientific exhibit of the American Medical Association held at Philadelphia, June 8-12, 1931, the hormone tests for early pregnancy were summarized in a pamphlet issued by P. Brooke Bland, Charles Mazer, Arthur First, and Paul Roeder.

The present concepts of the hormone tests for pregnancy are briefly as follows:

During pregnancy there is an overproduction of the gonad-stimulating hormone of the anterior pituitary gland

and of estrin or female sex hormone of the ovary, so that both hormones are excreted abundantly by the kidneys. The presence of these hormones in the urine is the basis of the 3 most important tests for early pregnancy.

**I Anterior Pituitary Sex Hormone Tests.**—*A Aschheim-Zondek Test*—This test depends upon the response of the immature mouse ovary to the anterior pituitary sex hormone content of 25 c c of whole urine. The routine steps carried out in the performance of this test are as follows.

1 *Inspection* of the animals as to immaturity.

(a) Weight 6 to 8 grams

(b) Closed vaginal introitus

2 *Identification* of the animals by painting them with carbolfuchsin

3 *Urine Injection*—The mouse is injected with 4 c c of the morning urine, 6 times in the course of 2 days. Three to 5 animals are simultaneously employed for 1 test.

4. *Daily Vaginal Smears*—Estrus, however, is not necessarily indicative of a positive test, because the female sex hormone, simultaneously contained in the urine, may be the responsible agent.

5 *Necropsy*—Four days after the first injection, or earlier if the animals are in estrus, they are killed with illuminating gas and the abdomen is opened for inspection of the ovaries *in situ* for hemorrhagic spots and yellowish protrusions. If there is no macroscopic evidence of follicular hemorrhage, or yellowish protrusion (corpora lutea), the ovaries are removed and prepared for serial sections.

6. *Microscopic Examination.*—The microscopic appearance of the infantile mouse ovary in its inactive state reveals numerous primordial follicles.

Reaction 1 shows the presence of ripening Graafian follicles due to the anterior pituitary sex hormone contained in the urine. This, however, is not indicative of pregnancy.

Reaction 2 shows the presence of hemorrhage into the follicles which may be seen macroscopically. This is positive for pregnancy.

Reaction 3 shows the presence of corpora lutea. This is also positive for pregnancy.

K. Ehrhardt (Surg. Gynec. Obst. 53:486 (Oct) 1931) reports on 2000 controlled Aschheim-Zondek pregnancy tests from the Women's Clinic, University of Frankfurt am Main. His results are decidedly encouraging. A correct diagnosis was made in 98 to 99 per cent of all patients. The mortality in the test animals was as high as 20 per cent, due in part to the toxicity of the urine and in part to the lack of resistance of the test animals. He insists that 5 mice be used for each test, but only kills 1 animal at a time. If the results in the first are clearly positive, it is not necessary to sacrifice the other 4 animals.

In 2 cases of hydatidiform mole the reaction was positive with  $\frac{1}{520}$  c.c. of urine and with  $\frac{1}{280}$  c.c. respectively.

After a transfusion of 500 to 700 c.c. of blood from pregnant women (1500 to 7000 mouse units of anterior hypophyseal hormone), he was able to demonstrate reactions 2 and 3 in the blood stream from 2 to 20 hours after the transfusion; soon after this the blood gave only a positive reaction 1, and still later the reaction was negative. Urine analysis demonstrated that the excess hormone was excreted, at least in its greatest part, in the first 24 hours in the urine. These results show that it is not advisable to work with large quantities of hypophyseal hormone for

therapeutic purposes, as an extra load will be excreted in the urine.

Reaction 1 is not significant in the diagnosis of pregnancy, for it may occur in the presence of slow, as well as rapidly proliferating, tumors (myoma or carcinoma), in the presence of diminishing genital function at the beginning of the menopause, and in certain types of amenorrhea.

Bland, Mazer, First and Roeder (*loc. cit.*) describe also the following tests:

*B. Rabbit Test (Friedman, modified by Schneider)*—This test also depends upon the presence of anterior pituitary sex hormone in the urine during pregnancy. The isolated rabbit is a convenient test animal, as it is more susceptible to the hormone and does not ovulate without copulation.

The routine steps carried out in the performance of this test are as follows:

1 *Isolation* of the animal for 3 weeks.

2 Seven to 10 c.c. of morning urine are injected into the marginal ear vein of the isolated rabbit.

3 Thirty hours thereafter a dorsal skin incision is made and 1 ovary is delivered through a lateral puncture wound. The presence of large hemorrhagic cysts (corpora hemorrhagica) is evidence of a positive reaction. The skin flaps are then closed and the animal is again employed for test purposes within a month. The presence of unruptured follicles, regardless of their size, denotes a negative reaction, in which case the other ovary should also be inspected. This technic is economical and obviates the need of carrying a large stock of animals.

**II Female Sex Hormone or Estrin Test (Mazer-Hoffman).**—This test depends upon the fact that varying quantities of follicular or female sex hormone are found in the urine of

pregnant women as early as 1 week after the first missed period. Three adult castrated mice are injected with 2 c.c. of boiled urine 6 times consecutively in the course of 2 days. The succession of changes in cell types, which are found in the vaginal lumen of sexually active white mice during the estrual cycle, is reproduced in the castrated test animals by the female sex hormone content of the urine.

The following routine steps are carried out in the performance of this test:

- 1 *Identification* of the female mice by painting them with carbolfuchsin.

2. *Inspection* of the animals as to maturity.

- (a) Weight 20 to 25 grams

- (b) Open vaginal introitus

3. *Vaginal Smears*.—Sexual activity of the white mouse is determined by daily vaginal smears taken with a platinum loop. One per cent thionin is used as a stain. Under proper environment estrus occurs every 4 to 6 days. Senile animals should not be employed.

The vaginal smear of the mouse during the resting phase of the estrual cycle shows many polymorphonuclear leukocytes and mucus.

The vaginal smear during the proestrus phase shows a preponderance of small nucleated epithelial cells and denotes activity in the vagina. It is then necessary to examine the vaginal secretion 2 or 3 times daily in order not to overlook an estrus phase.

The vaginal smear of the estrus phase shows a preponderance of large non-nucleated (cornified) epithelial cells and an absence of leukocytes and mucus.

4. *Castration*.—Animals which have shown one or more sexual cycles are castrated. The ovaries are removed by a dorsal incision. Castration is very

rapid (less than 5 minutes), and the mortality is less than 2 per cent. The removed tissues are immediately examined under the microscope to verify the complete removal of both ovaries.

- 5 *Daily Vaginal Smears*.—These are taken for 2 weeks, in order to exclude the presence of an accessory ovary or regeneration of an overlooked fragment.

- 6 *Urine Injection*.—Twelve c.c. of a morning specimen of whole urine are injected subcutaneously, in 6 divided doses, into each of 3 castrated animals in the course of 2 days.

7. *Daily Vaginal Smears*.—A positive reaction (estrus phase) in any of the 3 animals is indicative of pregnancy. This is usually obtained 4 days after the first injection.

**Comparative Value of Tests.**—The importance of determining the existence of the gravid state, together with the varying conditions from which it must be differentiated, have been repeatedly emphasized in the past few years. With the recent advent of the hormone tests for early pregnancy, a great deal of confusion, which hitherto confronted even the most skilled obstetrician, is today being clarified in the laboratory.

A report from the Jefferson Medical College Hospital by P. Brooke Bland, Arthur First and Paul Roeder (Am. J. Obst. Gynec. in press) is based upon a study of 243 patients, of whom 200 were problem cases, and 13 involved the question of life or death of the ovum. Many of the urine specimens were sent in by outside physicians, so that it was not always possible to secure a fresh morning specimen so essential for the test. Only those cases which were followed up, and in which an accurate report as to the outcome was obtained, were considered in this communication, thus adding to the value of this research.

In their conclusions they find that:

1. The anterior pituitary hormone *test of Aschheim and Zondek* is a reliable laboratory adjuvant for the diagnosis of early pregnancy. In their hands it yielded 82.4 per cent. correct positives and 93.2 per cent. correct negatives. The finding of 6.8 per cent. false positive results detracts, somewhat, from its complete reliability. Especially is this error likely to be encountered in women who are functionally sterile, due to endocrine disturbances, or in women approaching the menopause. In these women, a compensatory hypertrophy of the anterior hypophysis may produce an excessive quantity of hormone, which, finding its way into the urine, will render an incorrect positive.

Fluhman has shown that normal fertile women, and those suffering from hypofunction of the anterior hypophysis, rarely, if ever, have a demonstrable quantity of anterior pituitary hormone in the blood except during pregnancy.

According to Rowe and Lawrence, primary anterior pituitary hypofunction is nearly 5 times more frequent than either primary ovarian or thyroid hypofunction. Fluhman, however, found a demonstrable quantity of anterior pituitary sex hormone in the blood of castrated women and in those in whom the natural menopause was well established.

Pituitary hypertrophy following castration in the human was previously noted by Tandler and Grosz, evidently in an attempt to stimulate a poorly functioning ovary. Experimentally, Evans and Simpson and Engle have shown that the hypophysis of gonadectomized animals possesses an activity 5 times greater than the normal animal.

In a group of 18 sterile women suffering with amenorrhea, but without

any evidence of pelvic pathology, Mazer found 8, or 44.4 per cent., showed a demonstrable quantity of anterior pituitary hormone in the blood. In a study of 30 women suffering with delayed or scanty menstruation, he found the hormone in the blood in 6, or 20 per cent. Among 13 women in the early menopause, 7 positive reactions for anterior pituitary hormone in the blood were obtained, due, perhaps, to the hypertrophic changes in the gland. It is easily conceivable that this abnormal excess of hormone in the blood might also appear in the urine, so that these women may yield a falsely positive Aschheim-Zondek test for pregnancy.

2. The female sex hormone *test of Mazer* yields a smaller percentage of correct positives, but is somewhat more reliable in the positive diagnosis of pregnancy, especially in patients suffering with functional disturbances. A smaller percentage of false positives among nonpregnant patients (none in their series) was observed when this test was employed. This is probably due to the fact that hyperfunction of the ovaries, which would be necessary in order to produce an excess of female sex hormone in the urine and render a false positive, is rarely, if ever, found in cases of endocrine dysfunction.

3. In those patients in whom there is a question of a dead fetus (missed abortion), the presence of a positive Aschheim-Zondek and a negative Mazer test, on repeated occasions, denotes that the fetus is probably dead. It appears that the female sex hormone disappears from the urine somewhat earlier than does the anterior pituitary hormone.

4. Repeated negative Mazer tests in pregnancy in those cases accompanied by slight bleeding, denotes an insufficient quantity of female sex hormone

and a threatened abortion. Only when the female sex hormone appears in demonstrable quantities in the urine, can it be felt that the ovum has secured a firm location and that the pregnancy will go on uninterrupted.

A sound physiological explanation may be offered for this phenomenon. The function of the corpus luteum in producing an endometrium-sensitizing, ovulation-inhibiting hormone is today well established. It is also recognized as the chief source of estrin or female sex hormone in the early part of pregnancy, to be supplanted later by the placenta. Through the influence of the corpus luteum, the uterus is brought into a pregravid condition, in preparation for the reception of the fertilized ovum. During pregnancy, the corpus luteum inhibits follicular ripening, as well as the cyclic engorgement of the genitals, which might disturb the developing ovum. If fertilization fails to occur, however, or the fetus dies, regressive changes in the corpus luteum or placenta have either already occurred, or take place immediately thereafter. The source of supply of the female sex hormone is thus instantly severed, and the Mazer test for pregnancy, which depends upon the activity of this hormone, is rendered negative.

The withdrawal of the hormonal production of the anterior pituitary gland appears, however, to be more delayed after the fetus is no longer viable. Although the ovum may be dead, as long as living syncytial cells or trophoblastic elements are present in the walls of the uterus, they either produce anterior pituitary hormone themselves or continue to stimulate the anterior pituitary gland. This is the explanation for the positive Aschheim-Zondek reaction after the expulsion of a hydatid mole. This

may also explain the occurrence of a positive Aschheim-Zondek reaction and a negative Mazer test in 4 patients who eventually were proved to have an inevitable abortion.

5 The larger percentage of correct positives with the Aschheim-Zondek test, and the smaller percentage of false positives with the Mazer test, suggests that both tests be simultaneously employed in each case in order to yield the most accurate results.

M. R. White and A. O. Severance (J. A. M. A. 97:1275 (Oct. 31) 1931) summarize their results with the various biologic tests for pregnancy as follows:

In 191 *Aschheim-Zondek reactions* there were 20 instances in which the result did not check with the final diagnosis. There were 5 false positive reactions among 69 controls which were not pregnant. There were 29 observations in a group of ectopic pregnancies and incomplete abortions, 14 of which were negative. In only 1 case of pregnancy was the Aschheim-Zondek reaction negative.

The *Brouha reaction* was uniformly positive in a group consisting of 60 normal pregnancies, 10 ectopic pregnancies and 9 incomplete abortions. There were 10 false positive reactions in a series of 27 nongravid women. Four of these showed hypertrophy of the endometrium, 3 complained of menstrual irregularity, and 1 had tuberculous salpingitis. (In this test 4 male mice weighing from 8 to 15 Gm. each, are injected with from 0.1 to 0.4 cc. of morning urine daily for from 8 to 10 days. They are killed 24 hours after the last injection. The reaction is positive for pregnancy if the seminal vesicles are abnormally enlarged, swollen, and distended with a whitish fluid.)



The *Friedman test* was observed in 40 cases. In the groups of normal pregnancies and nongravid controls there were 32 observations, all of which were correct with 1 exception. In this case, which proved to be a normal pregnancy, the reaction was carried out on the thirty-second day after the last menstrual period. There were 4 ectopic pregnancies, which gave 2 positive and 2 negative reactions. There were 4 incomplete abortions, 3 of which gave positive reactions.

The tests of Aschheim and Zondek and of Brouha gave false positive reactions which probably depended on some endocrine disturbance. In such cases a consideration of the history usually prevents confusion.

In the groups of ectopic pregnancies and incomplete abortions, the Aschheim-Zondek reaction was of value as a diagnostic procedure in 51 per cent of the cases, whereas the Friedman reaction was of diagnostic value in 62 per cent of the cases. The Brouha reaction was uniformly correct, however, this reaction does not lend itself as a practical diagnostic aid in cases of this type because of the time required for carrying out the test.

In cases of suspected normal pregnancy the Brouha reaction possesses distinct advantages over the Aschheim-Zondek reaction in that the results are determined macroscopically, and nearly mature test animals may be used.

The advantages of the Friedman reaction are that only 1 test animal is required and that the reading may be made macroscopically at the end of from 24 to 48 hours. These authors believe that the Friedman test is a dependable biologic reaction and a suitable laboratory procedure.

The tests of Aschheim and Zondek,

of Brouha, and of Friedman depend on a quantitative change in the amount of active principle that is excreted in the urine during pregnancy. This active principle is presumably anterior lobe hormone. A substance specific to pregnancy has not been demonstrated.

In their experience, the *scrum test* of *Manoilov* and the *pupillary reaction* of *Bercovits* have been of little value as diagnostic aids.

### PRURITUS ANI.—ETIOLOGY.

—In discussing the relationship of irritation and trauma to the nerves in the etiology of pruritus ani, J. F. Montague (M. J. and Rec. 132:272 (Sept. 17), 1930) quotes Mueller, who believes that "any sensation induced by external causes may, in the absence of such causes, still be induced by intrinsic changes in the nerves themselves."

The perineal area is innervated by branches from the dorsal roots arising in the first, second, third and fourth sacral segments, being part of the pudendal plexus. These segments are in close relation with the viscera of the abdomen and pelvis, sending rami communicantes direct to these viscera, and maintain an intimate connection between the hypogastric and aortic plexuses and those of the superior and inferior mesentery. An understanding of these nerve connections and relations is of importance in connection with the etiology of those obscure cases of pruritus in which no local manifestations are in evidence. It has a wide variety of causative factors. In 128 cases 20 different pathological conditions were found to exist in the rectum. In other cases it was due to chronic conditions wholly unrelated to the lower bowel.

It is not a disease *per se*, but a symptom. Every case of pruritus ani has a

cause and this must be sought out and remedied. A thorough and complete physical examination should be made. Whenever an abdominal or pelvic organ is in a state of congestion or inflammation, or is distended or hypertrophic for any reason, the visceral nerves involved will carry afferent stimuli to the central nervous system, and when these stimuli are not of a painful nature, they may still be capable of being transferred through related nerve paths and interpreted as anal itching. Because the viscera are innervated by autonomic nerves incapable of conveying pain, this is the only reaction possible.

In a study of 350 cases anorectal affections were in the majority. Ovarian cysts and prostatic disease are especially likely causes. Stricture and cancer of the rectum were discovered in 11 of these cases. Exploration with the rectosigmoidoscope should never be omitted.

**TREATMENT.**—Severe secondary infection from scratching sometimes needs treatment. Where there is denuded surface, 10 per cent. **silver nitrate solution** may be used to cauterize the lesions. The surface should be protected by some **bland ointment**.

As a measure to permit healing of trauma, the operation of **undercutting** is recommended.

**PSORIASIS.—TREATMENT.**—A new form of therapy for psoriasis has been used by H. Sutherland-Campbell and Kendal Frost (Arch. Dermat. and Syph. 22:685 (Oct.) 1930) in 15 cases who were treated by intramuscular injections of a suspension of the patient's own finely ground psoriatic scales in alcohol, *i.e.*, 20 Gm (5 drams) of scales to 20 c.c. (5 drams) of pure alcohol. Dosage from 1 to 4 c.c. (15 to 60 minims) at intervals of 4 days.

No untoward effects resulted. All the patients responded to this form of therapy, but in varying degree. The objective changes to occur are common to all, but the period of time varies fairly widely.

1 A thinning of the scales, which become less adherent. 2 A gradual paling of the center of lesions. 3 The last stage shows a smooth, slightly discolored area the size of the lesion.

The technic for the treatment of psoriasis, as used at Mayo Clinic, is reported by W. H. Goeckerman (Arch. Dermat. and Syph. 24:446 (Sept) 1931) as follows:

Patients with psoriasis are usually hospitalized when they come to Mayo Clinic, because most of them come from a considerable distance and hospitalization permits more perfect control of the details of technic. This, however, is not necessary, and under many conditions ambulatory treatment may be preferable.

Under hospital conditions, an ointment containing from 1 to 5 per cent **crude coal tar** is applied about  $\frac{1}{8}$  inch thick to the various patches, whether large or small. The formula for this ointment is as follows: crude coal tar, from 0.5 to 1.5 drams (2 to 6 Gm.); zinc oxide, 1 ounce (30 Gm.); and enough petrolatum to make 4 ounces (120 Gm.).

The ointment is permitted to remain on the patches until the next day, up to the time at which the technician who operates the air-cooled **quartz lamp** is ready for the patient's exposure. The excess of the ointment of crude coal tar is then removed with olive oil; a thin film, enough to look like a brown stain, is purposely allowed to remain. These stained patches are then exposed to the quartz lamp, beginning with a light exposure, so as to avoid any particular re-

action from the light. With the ordinarily employed well functioning lamp, a beginning exposure of 1 minute at a distance of 30 inches is practicable. The exposure is given daily and is lengthened by half a minute until from 4 to 5 exposures have been given. The average patient has now acquired considerable tolerance, and the time of exposure may be lengthened rapidly and the distance shortened. There is no necessity for producing severe erythema, gradual tanning is the object desired. The quartz lamp should be in proper order, and persons sensitive to light should not be exposed to the light too long or at too short a distance. Following exposure to the light, the patient is permitted to take a bath with soap and water, or, if his skin is sensitive, an oatmeal and soda bath. In order to give the patient a few hours of comfort, the ointment is not reapplied for several hours. The whole procedure is repeated daily. Mild conditions clear up in from 2 to 3 weeks and severe conditions in from 3 to 4 weeks.

The treatment given ambulatory patients is in all essentials the same as that given patients in the hospital, minor points are modified to meet the convenience of the patient, and to permit him to continue his ordinary occupation. The ointment is applied at bedtime and is removed in the morning, the patches are exposed promptly, a cleansing bath is taken, and the patient is not hampered by uncomfortable applications during the day. It is desirable, of course, that the patient use old underwear and bed clothing during the course of treatment, although the tar is not permanently injurious to clothing. While the glabrous skin is being treated by the tar and light, the *scalp* and *nails*, in event of their involvement, are treated by 20 per cent.

ointment of ammoniated mercury. This is thoroughly rubbed in and can be readily removed by soap and water.

Since psoriasis varies so much in its clinical behavior in different cases, and even in the same case in different attacks, it always has been difficult to evaluate the merits of any particular method of treatment. The literature is replete with suggestions that have succeeded in a few cases but that have failed when put to a critical test. Therefore, it seems desirable to review in some detail the cases of patients treated systematically at The Mayo Clinic by coal tar and ultraviolet light since Jan. 1, 1925. From that time until Nov. 20, 1930, records of 936 cases of psoriasis have been made. In this series, 181 patients received one or more systematic courses of treatment. In 3 cases the treatment failed. In 133 cases (14 per cent) the psoriasis was associated with arthritis, in this group, 40 patients were treated. There were, among the total number, a group of 28 cases of exfoliative dermatitis secondary to the psoriasis, and in 19 of these treatment was given.

Most of the patients did not come to the clinic for consideration of the psoriasis. It was often of no significance, since there were many among them with generalized carcinomatosis, tumor of the brain, and other severe organic nervous diseases, exophthalmic goiter, severe abdominal surgical lesions, and other conditions. The comparatively small number treated in proportion to the large number seen is, therefore, to be expected. Two of the 3 patients who did not respond to treatment had a rather strange type of the disease. One of these 2 patients, a man aged 44, had patches of psoriasis chiefly involving the hands and feet, including

the nails, and also patches over the trunk and extremities. Pain in the extremities was severe, and hyperhidrosis of the hands and feet was marked. Arthritis was not present, and the general health was fair, except for the psoriasis. The other of these 2 patients, a man aged 40, had marked involvement of the feet, hands, and wrists, including the palms. Severe arthritis varied in direct proportion to the course of the psoriasis. Aside from this, the patient's general health was good. In the third case of the 3 in which treatment was not effective, the disease was not of unusual type. The patient was a man, aged 23, with large patches of psoriasis distributed chiefly over the trunk and lower extremities. The nails were not involved. The patient's general health was good. No explanation can be offered for the failure in treatment.

About one-fourth of the patients who were treated received more than 1 course and several received 3 or 4 courses, 1 patient received 5 separate courses at intervals. The response was equally good. A patient who responded unusually rapidly the first time would do so subsequently, conversely, a slower response in a patient would be repeated. The intervals of freedom from eruption varied from a few weeks to several years, in this respect, the treatment does not differ from other methods. That direct treatment for the cutaneous patches by external measures can do no more than cause their disappearance seems quite evident. It is probable that psoriasis has a metabolic background, and this method of treatment was not intended to cause a profound impression on the course of the disease.

In the 40 cases of *psoriasis with arthritis* in which treatment was given, the fact was evident that as the cutaneous

patches disappeared, the arthritis improved. It was as though the psoriatic patches contained or elaborated a substance that aggravated the arthritis. The psoriasis responded as readily as in the cases without arthritis, but in only about half of the cases can it be said that the arthritis responded as the result of the treatment for the cutaneous patches. It was impossible to determine whether the arthritis was part of the psoriatic process in all of the cases. Many of the cases were typical of arthritis which slowly develops in the later years of psoriasis and which often produces pronounced deformity and general incapacity, and every effort was made to include only cases to which the term "arthritis psoriatica" might be applied. This is difficult, owing to the ill-defined character of chronic arthritis and the unknown etiology of psoriasis. That arthritis should have existed before there were cutaneous manifestations does not necessarily mean that the arthritis psoriatica will respond to treatment for the skin patches in some cases, but that lack of response does not indicate that the arthritis is of a different type from that known as arthritis psoriatica. There is still an unknown factor that determines the variation in the response. However, these conclusions are based on only 40 cases in which treatment was given, and it is possible that a large series, intensively studied, might modify these observations.

In the 19 cases of *exfoliative dermatitis* secondary to psoriasis in which treatment was given, the response to treatment was the same in time and manner as the response of psoriasis by itself. A series of 19 cases is not large, but considering the uniformly good results, especially when contrasted with the course of events in the 9 cases in

which other measures of treatment were used, the value of the method is evident. It is especially in this group, so often exceedingly refractory to treatment, that the unique efficacy and value of the method have made itself evident as experience has increased.

In conclusion the writer states that the use of tar and ultraviolet light in the treatment for psoriasis is the outgrowth of a persistent effort, not to "cure" but more effectually to control individual attacks. There is no evidence that this treatment will in any way fundamentally modify the course of the disease. Intervals of freedom from eruption are probably not determined by it. Psoriasis associated with arthritis responds symptomatically as well as psoriasis without arthritis. For some unknown reason, the arthritis is materially benefited in about half the cases by treating the lesions of the skin. A small percentage of cases with rather distinctive clinical manifestations does not respond well to treatment. Its beneficial effect in exfoliative dermatitis secondary to psoriasis is unique. It is not recommended as a measure to be applied as a routine for a few patches of psoriasis, as other efficacious methods are more simple, but it can often be used without materially interfering with the patient's work. The scalp and nails do not lend themselves to this method of treatment. It is a decidedly valuable method for clearing up temporarily extensive and resistant eruptions on the glabrous skin, and practically always succeeds when various forms of treatment by x-rays, chrysarobin or other substances and methods have failed or are contraindicated. The principles of the treatment must be applied and the simple technic mastered, or success cannot be expected.

**PURPURA.** See ALLESTON.

**PYELITIS.—ETIOLOGY** — Experimental work carried out by Helmholtz (Brit J Child Dis 26: 247 (Oct-Dec) 1929) upon rabbits showed that the frequency of infection of the bladder as compared with the upper portion of the urinary tract and the fact that the colon bacillus, after intravenous injection did not persist in the bladder when the upper portion of the urinary tract was sterile, seemed to indicate that the infection was of the ascending type.

In the clinical stage, the higher incidence of infection of female infants during the diaper period is still the outstanding feature in the determination of the mode of infection. Schwartz has found that bacilluria is twice as common in female as in male infants. David and McGill showed that colon bacilli appear in the blood stream only after complete obstruction of the bowel. Even when colon bacilli are injected into the circulation, they do not appear in the urine, according to the author.

**TREATMENT.**—The beneficial results obtained from the use of alkalis in the treatment of pyelitis has not been satisfactorily proven. It is certain that the degree of alkalinity attained in the urine is not sufficient to retard the growth of the colon bacillus. No differences could be detected when the bacilli were grown in either an acid or alkaline medium. In a series of therapeutic experiments carried out on animals in which they were infected hematogenously with colon bacilli, and in which mercurochrome, methenamine and hexylresorcinol were administered, by far the most satisfactory results were obtained with methenamine.

In concluding his article Helmholtz (*loc cit*) states that it is essential

to check bacteriologically every case of pyelitis before a cure can be pronounced and that cases which do not clear up following an intensive course and sufficient administration of methenamine should be referred to the urologist for more careful study of the urinary tract

C Lepoutre (Arch d mal d reins 4 624 (Apr) 1930) reports a series of cases in which he deals with only those which show no gross changes requiring surgical treatment and describes in detail nearly all of the various medical treatments that are employed, *i e*, hygienic, dietary, hydrotherapeutic, antiseptic, local and biological, each with their special indications

**Alkalinization** is of extreme benefit, but avoidance of potassium salts should be kept in mind, since they aggravate a diarrhea. The administration of **sodium bicarbonate** in large quantities has little effect upon the pyuria but usually relieves the general symptoms

Lepoutre believes **urotropin** to be the most effective urinary antiseptic. As it acts only in an acid urine, it should be combined with **phosphoric acid** or **sodium benzoate**. The dose should not exceed 2 Gm (30 grains) per day, because of the irritating effect of the formaldehyde and the possibility of a hematuria

The favorable effect of **lavage of the bladder** on pyelitis was first noted by Guyon. A tepid solution of water or boric acid is injected very slowly through a soft rubber catheter until discomfort is experienced. After a few minutes the catheter is removed and the patient allowed to urinate. **Lavage of the kidneys** also gives excellent results

The question of the administration of **vaccine** is a mooted one and the pendulum is swinging from the former opinion of a specific immunity being built there-

by, to a more modern version of the thought that the immunity is more a local phenomenon. However, those vaccines which cause a nonspecific phenomenon of shock may be of therapeutic value

In using the **bacteriophage**, a strain must be employed which is adapted to the invading organism. From 2 to 3.3 c c are injected subcutaneously every other day. The maximum number of doses is 4. At the same time, from 10 to 20 c c are given by mouth and a like amount is injected into the bladder to be retained as long as possible

### **PYELITIS IN CHILDREN.—**

Pyelitis, according to S H Harris (M J Australia 2 448 (Sept 27) 1930), is an extremely uncommon condition as a *disease entity*, the author stating that the majority of patients with symptoms of this disease are undoubtedly suffering from a much more tangible lesion. "Pyelitis" is consequently looked upon by Harris merely as a symptom or indication of disease and not as a diagnosis

**INCIDENCE.**—A S Hurt, Jr (Am J Dis Child 40 1374 (Dec) 1930) observed a group of 773 babies throughout the period of infancy. Eleven infants, or 1.4 per cent, had pyelitis at some time during the first 2 years of life

**ETIOLOGY.—Predisposing Causes.**—The generally recognized influence of both *sex* and *age* upon the incidence of pyelitis is again emphasized by recent observations. In a series of 75 cases of pyelitis in children studied by D D Martin (J Florida M A 16. 256 (Dec) 1929) only 1 occurred in a male patient, while of a group of 11 cases of pyelitis occurring in the first 2 years of life studied by Hurt (*loc cit*), 10 occurred in female patients. The



necropsy records of the Royal Hospital for Sick Children during 15 years contained 160 cases, of which 113 were female patients and 47 male. One hundred of the female patients and 43 of the male were within the *second year* of life, according to M. A. Griffin (Glasgow M. J. 114 21 (July) 1930). A. V. Neale (Arch. Dis. Childhood 6 165 (June) 1931) observed that the pyelitis in some instances would seem to follow definite disease elsewhere, *i.e.*, *otitis media*, *bronchiolitis*, *gastroenteritis*.

**Anomalies** of the urinary tract are being given increasing attention in the etiology of pyelitis. Of the 11 cases studied by Hurt (*loc. cit.*), 2 infants, or 0.25 per cent had anomalies of the urinary tract. However, H. F. Helmholtz (Am. J. Dis. Child. 40 1374 (Dec.) 1930) states that anomalies do not predispose to infection, but if infection settles in the urinary tract that has an anomaly interfering with free drainage of the urine, the case is likely to resist medical treatment unless the anomalous condition can be corrected. Urinary stasis may be caused by obstruction within the urinary tract itself, that is to say, of *intrinsic* type, or by pressure from without, that is, of *extrinsic* type, Harris (*loc. cit.*)

**Intrinsic obstruction** in children and infants may be due to various types of congenital obstruction at the bladder neck, the prostatic urethra, and the like. Another type which Harris has named "renal sympatheticotonus," is due to over action of the sympathetic nerve supply of the kidney. Spasticity of the muscles, with incoordinations of the contractions of the pelvic calyces and ureter, is thus induced with resulting increased intracalycal and intrapelvic tension. The condition, according to Har-

ris, is often associated with a generalized sympatheticotonus, sometimes actually localized to the side of the renal lesion, as manifested by increased excitability of the knee jerks and delayed relaxation time. The condition also accounts for some types of hydronephrosis.

**Extrinsic Causes**—According to Harris, of the extrinsic causes, the most common are obstruction bands, kinks or aberrant vessels at ureteropelvic junction and upper third of the ureter. Obstruction at the ureteropelvic junction is said probably to be the most common cause of hydronephrosis, and quite frequently an advanced grade of hydronephrosis is present before infection supervenes.

**Specific Causes.**—Among 60 cases of pyelitis examined bacteriologically, Griffin (*loc. cit.*) reported that various members of the *Bacillus coli* group were found alone in 38, streptococci alone in 7, and both coliform and streptococcic organisms in 15 cases. In 17 cases the patient's serum was tested for agglutination and antibodies against the organisms isolated from the urine, and in 8 cases agglutination occurred. The patients whose serum in high dilution agglutinated the infecting organism were generally acutely ill, whereas those whose serum did not agglutinate the microorganism found in the urine had less severe clinical symptoms.

B. Vasile (Pediatria 36 113 (Feb. 1) 1928) described 9 cases in children aged from 6 to 18 months suffering from *B. coli* infection of the urinary passages. The strains isolated were inoculated into guinea-pigs. It was possible to isolate strains from the animals which were identical with those obtained from the patient, and other strains which had lost some of their characteristics. Such modifications were more or less marked and by passage through animals the for-

mer properties were regained. Consequently those strains were not looked upon as belonging to a separate group, but were considered as strains which had undergone modification in their biologic characteristics during the period of parasitism. Such changes were thought to be due to immunization phenomena. Out of 9 cases observed, agglutination of the strains isolated from the urine with the blood serums of the same patient was positive only in 5 instances. R. D'Aunoy (Am J M. Sc 178 834 (Dec) 1929) observed 3 cases of pyelitis, 2 of which were in children 3 years of age, apparently caused by *Morgan's bacillus*. Agglutinins were demonstrated for homologous organisms in the blood of all 3 patients.

According to H. F. Helmholz (Brit J Child Dis 26 247 (Oct-Dec) 1929), cultures of urine from most normal infants are sterile. However, if divided portions of the urine are cultivated it is observed that the first portion is much more likely to contain bacteria than the others, indicating that in all probability bacteria are often carried into the bladder with the catheter. M. Solis-Cohen (Am J Dis Child 39 1356 (June) 1930) contends that most of the theories in regard to the etiology, pathogenesis and treatment of pyelitis are based on ordinary cultures of the urine. The author has shown, and others have confirmed, that when simultaneous cultures are made on ordinary media and on the patient's fresh whole blood, organisms growing on the former are absent on the latter, and *vice versa*. Organisms able to grow in the patient's blood are believed to be pathogenic for him, while those unable to survive in it are regarded as nonpathogenic.

The *colon bacillus*, according to Solis-Cohen, frequently found in ordinary cul-

ture of the urine in cases of pyelitis and often regarded as the etiologic factor, failed to grow in the patient's blood in many instances, while streptococci or other pyogenic organisms not present or in small numbers in ordinary cultures of the urine, do grow when the urine is cultured in the patient's whole blood. In such cases, similar pyogenic organisms usually are also found in the upper respiratory tract, indicating the probable primary source of the infection.

**PATHOLOGY.**—In the study reported by Griffin (*loc cit*), the infection was found to be bilateral upon necropsy examination in 15 of the 160 fatal cases with pyelitis. A definite cystitis was present in 70 cases. In these fatal cases the pyuria was generally due to a pyelonephritis rather than to a simple pyelitis. In the majority of cases the urinary bladder and the renal pelves were usually much less severely affected than the kidney substance which showed cellular reaction, chiefly in the cortex with microorganisms in the glomeruli and blood vessels. Severe renal disease was also found in the severe fatal cases reported by Neale (*loc cit.*). In most instances suppuration in the kidney substance with considerable destruction of tissue was present, or the initial condition was congenital hydronephrosis with atrophy of the renal cortex and an acute suppuration added. However, the kidneys, ureters and bladder of 1 acute case of pyelitis dying 2 weeks after recovery from the disease were found to be entirely normal in appearance.

**Portal of Entry.**—Neale (*loc cit*) states that probably the 2 important routes by which the renal tract becomes infected are: (a) the *ascending*, from the urethra and bladder, and (b) the *hematogenous*, he thinks (c) the *lateral*

spread from such conditions as appendicitis or enterocolonic conditions is unlikely, although *B coli* bacteremia or septicemia may so arise and cause infection in the urinary tract. He points out that it has been recently shown that so-called catheter fever is due to actual invasion of the blood stream by coliform bacilli after slight ureteral trauma. From the necropsy findings reported by Griffin (*loc cit*) and by Neale (*loc cit*), the evidence seems to favor a blood-borne infection, at least as far as the fatal cases are concerned.

H F Helmholtz (Brit J Dis Child 26:247 (Oct-Dec) 1930, Am J Dis Child 4:1374 (Dec) 1930) has produced experimental pyelitis in rabbits both by intravenous and intracystical injections of *B coli*. He concludes that the frequency of infection of the bladder as compared with infection of the upper portion of the urinary tract, together with the fact that the colon bacillus after intravenous injections does not persist in the bladder when the upper portion of the urinary tract is sterile, would seem to indicate that in the rabbit the infection is of the ascending type. On the clinical side, the predominance of the infection of girl babies during the diaper age is still the outstanding feature in the determination of the mode of infection, to which must be added the studies of Schwartz, who found that bacilluria is twice as common in girl babies as in boys.

**SYMPTOMATOLOGY.—Acute Nonfatal Pyelitis.**—In infants, according to Neale (*loc cit*), the clinical aspect is that of moderately severe illness, with marked pyrexia and rapid loss in weight, frequently preceded, accompanied or followed by such gastrointestinal disorders as diarrhea, vomiting, dehydration and ketosis. Often

there is little to indicate renal tract disorder, such conditions as *meningismus*, *twitchings*, *convulsions* and a *bulging fontanelle* attracting the physician's attention to the nervous system. Occasionally, abdominal distention and tenderness or definite loin pain may be present. Vulval, scrotal, or gluteal excoriations may be seen. In the earliest stages of some very acute cases the evidence of the renal tract infection may be little, but in a few days frank pyuria and bacilluria appear. Possibly this latter type of case may be due to an actual blood stream infection with the organism, which soon becomes localized in the renal tract.

In the older child the symptomatology is more often directly referable to the urinary system, the complaint varying from enuresis to a severe general febrile disturbance, with loin pain and tenderness, frequency of urination, dysuria and opalescent, hyperacid, urine.

**Chronic Pyelitis.**—In 7 of the 56 patients reexamined by Neale 2 or more years after treatment for clinical acute pyelitis, persistent pyuria was present. The condition of chronic pyelitis may be detected at the onset, in which case the clinical picture does not differ from ordinary acute pyelitis. In many cases the disease has been established a variable period of time when recognized. There may be no symptoms, although usually a complaint of intermittent loin or ureteric pain, enuresis, polyuria or febrile attacks may be present. The pyuria may occasionally be detected on routine urine examination. The frequent absence of general disturbance for some years is remarkable. The benign nature of the general effect is more evident in the cases where pyuria is due to unilateral renal and ureteric diseases. The cases of unilateral infection may, un-

doubtedly, continue for many years. Provided no acute spread of this suppurative process into the renal substance or sudden dispersion of infection throughout the renal system takes place, no untoward symptoms occur. The physical effects of chronic infection are more marked in cases showing bilateral renal tract infection. When both kidneys are diseased, a slow progressive deterioration of kidney function is evident with gradual nitrogen retention. A remarkable feature of the disease is the postponement of any serious renal failure until very little kidney tissue remains.

Chronic pyuria is nearly always associated with congenital anatomical defect in the renal tract which impedes the normal peristaltic movement and drainage, Neale (*loc cit*). In nearly all cases of chronic suppuration in the renal tract, the primary focus of the disease lies in the supravescical portion, in the ureter and renal pelvis. Very rarely the chronic infection is due to some abnormality in the bladder, such as a congenital diverticulum or urethral mucosal valve, producing deficient bladder action, or it is associated with disease in the nervous system.

**Blood.**—According to Martin (*loc cit*), in relatively severe cases the leukocyte count is nearly normal with a normal polymorphonuclear count. The count is proportionately higher in mild cases than in severe cases.

**Kidney Damage.**—In only 1 or 2 of the acute nonfatal cases of pyelitis reported by Neale was there visible edema. The urinary findings would not lead to the diagnosis of nephritis—the albumin content is usually small, casts are nearly always absent, although a few red blood cells may appear, and polymorphonuclear leukocytes are in abundance, to-

gether with the infecting coliform bacilli. The volume of the urine may be normal or diminished when hyperpyrexia is present. However, the blood urea may be raised soon after the onset of the disease, indicating that there is some temporary renal impairment. A suppurative process extending into the renal substance renders the prognosis bad, but the only significant differential clinical features indicating this extension are diminished excretion of urine, persistence of pyuria and, in some cases, a continued severe febrile disturbance with progressive physical deterioration.

**DIAGNOSIS.**—J. N. Cumings (Brit. M. J. 1 305 (Feb. 21) 1931), using the ordinary counting chamber, made urinary white cell counts on normal male and female children, as well as on those with cystitis and pyelitis. The enumeration of pus cells by this method, the author points out, might be widely adopted, as it furnishes an accurate means of following the progress of a case from day to day and of comparing one patient with another. The author concludes that in boys as many as 10 cells per c mm can be considered as being within normal limits, in girls as many as 100 c mm. Cumings's standard of the upper limit of normal for female patients is considerably higher than previously determined by Friedman and Mitchell (see Sajous's Supplement, 10 748, 193).

**Intravenous Urography (Uroselectan)**—Certain difficulties are met with in applying the usual surgical procedures in children in investigating the cause of protracted or chronic cases of pyelitis. While cystoscopy usually presents no difficulties, pyelography by ureteral catheterization may be extremely difficult or impossible to carry out. The cystogram, according to Neale, is useful occa-

sionally, and ureteral reflux is shown in some abnormal conditions of the tract, but distortions and dilations of the upper parts of the ureter and renal pelvis are not shown. By the use of intravenous injections of uroselectan followed by radiography, a very useful method of investigating the renal tract is now available. M. Swick (*Am J Surg* 8:405 (Feb) 1930), J. C. McClelland (*Canad M A J* 24:213 (Feb) 1931), Neale (*loc cit*), T. H. Lanman and P. J. Mahoney (*Am J Dis Child* 42:611 (Sept) 1931).

*Uroselectan*, according to McClelland (*loc cit*), is a derivative of pyridine, with 42 per cent iodine in chemical combination. It is the sodium salt of 2 oxy—5 iodopyridin—N-acetic acid. It is readily soluble and is eliminated by the kidneys in sufficient concentration to give an outline of the urinary passages upon x-ray examination. The amount of uroselectan eliminated is dependent upon the kidney function. Thus, a good picture means good function, a delayed picture means delayed function. The concentration of the uroselectan elimination is about 5 per cent and will not give so intense a picture as the 12 per cent sodium iodide used in instrumental pyelography. While uroselectan is generally considered as nontoxic, even in large doses, it probably should not be administered to those patients with considerable kidney damage, as Swick (*loc cit*) and Lanman and Mahoney (*loc cit*) reported instances in which death occurred in patients of this type following the injection of uroselectan.

According to Swick, the adult dose of *uroselectan* ranges between 33 and 40 Gm (1 to 1½ ounces) dissolved in 100 cc (3½ ounces) of doubly distilled water. The solution is filtered twice through ordinary filter paper and steril-

ized in a water bath or autoclave at 15 pounds pressure for ½ hour. A child of 7 years receives one-half and a child of 2 years, one-quarter of the adult dose. The injection is done in 2 stages at intervals of 3 to 5 minutes. The first x-ray examination is usually made about 15 minutes after the last injection, the second about 20 to 30 minutes after the first x-ray plate and the third a corresponding period after the second. The number of subsequent plates and the time at which they are taken depends upon the functional activity and derangement of the kidney. During the injections the patients experience transient thirst, and also generalized warmth particularly involving the face and bladder region. Nausea, vomiting and shivering less commonly occur.

Urography by intravenous methods is a valuable adjunct in the diagnosis of disease of the urinary tract. For purely mechanical reasons concerning the technic of the operation, intravenous urography in children is superior to that obtained by ureteral catheterization. Furthermore, according to McClelland, uroselectan will outline a pelvis and ureter when some mechanical obstruction is present which prevents sodium iodide reaching the kidney pelvis when introduced through the catheter. However, pyelograms with uroselectan are not so sharply defined as with sodium iodide. Furthermore, Lanman and Mahoney point out, the value of intravenous urography is limited in cases showing a marked degree of pyuria associated with damage of the kidney, a group of cases comprising about 60 per cent of the disorders of the urinary tract. Patients should be studied carefully, these authors contend, and all simpler means of diagnosis should be employed first and complete studies of renal function

should also be made. The general use of uroselectan in unselected and imperfectly studied cases should be avoided, both because of the expense and uncertainty of the information often obtained.

**PROGNOSIS.**—Neale (*loc cit*) has found that there is no progressive or permanent physical or renal impairment in the acute cases of pyelitis which respond rapidly to medical treatment, even though there may be a slight degree of impairment of kidney function in the acute pyrexial stage. Broadly speaking, the *older the child* the less is the probability of any serious involvement of the renal parenchyma. In *infants* and young children, however, a general spread of the purulent process into the kidney substance may take place and suppurative pyelonephritis supervene, which almost certainly renders the condition an extremely grave one. In all *fatal* cases of acute renal tract infections, postmortem examination has shown this change.

The remarkably good general condition of many children with chronic pyuria indicates that, in most instances, no serious renal dysfunction exists. The length of life under these conditions depends upon the absence or spread of infection to the renal secretory tissues.

**TREATMENT.**—**Bacteriophage**—C. Nyberg (Finska lak sällsk handl 72:926 (Nov) 1930) reports 3 cases of acute colipyelitis treated with bacteriophage with good results. The author states that in chronic cases it is difficult to find effective bacteriophages; frequently 2 or more strains of colon bacilli appear in the urine and each of these requires a special bacteriophage.

**Pituitary Extract.**—N. Ginsberg (M J and Rec. 131:28 (Jan 1) 1930) treated a stubborn case of pyelitis in a female child of 2 years by injections of

pituitary extract. In addition to the typical urinary findings, the child had been running a septic temperature ranging from 102° to 106° F (38.9° to 41.1° C) for a period of 26 days without responding to the usual therapeutic measures. Three minims (0.18 cc) of pituitary extract was then injected at a time when the temperature was 106° F (41.1° C). About 15 minutes following the injection the temperature fell to 100° F (37.8° C). Six hours later the temperature rose to 104° F (40° C), and again shortly after the injection of pituitary extract, the temperature fell to 100.5° F (38° C). Pituitary extract was then given every 2 hours in 2 minim (0.12 cc) doses. This treatment was immediately followed by a continued normal temperature and an uneventful convalescence. The urinary findings were found to be markedly improved about 48 hours after beginning treatment. The pituitary extract therapy was continued for 5 days. The author thinks the therapeutic action of pituitary extract lies in its power to contract smooth musculature, thus establishing better urinary drainage by increasing the tone of the ureters and bladder.

W. B. Draper, W. Darley and J. L. Harvey (J Urol. 26:1 (July) 1931) found that the intramuscular injections of pituitary extract and "pitressin" reduce the size and density of the pelvic and ureteral shadows as shown by intravenous urography. The shadow is thought to diminish because of accelerated drainage. The authors point out that while the therapeutic value of pituitary extract is still an open question, the results obtained are encouraging.

**Removal of Diseased Tissue.**—Solis-Cohen (*loc cit*) points out that in those cases of pyelitis secondary to upper respiratory infection, the pyelitis



cannot be cured until the diseased tissue in the upper respiratory tract has been removed and the patient's resistance to the infecting organism has been built up by carefully prepared vaccines.

In chronic pyuria associated with renal tract defect, alkalis, hexamine, pyridium, vaccine, bacteriophage and the like have all proved of little permanent value, according to Neale. Harris, too, states that treatment of persistent pyuria with vaccine and bladder irrigation without complete investigation of the patient cannot be too strongly condemned. Failure to recognize the fact is the reason that too many patients present themselves for urologic investigation at a time when any possibility of conservative treatment is long past. Neale has found that in chronic pyuria associated with renal or ureteral malformation, excision of the diseased part of the upper renal tract in unilateral cases has proven of permanent value. In bilateral conditions surgical measures are not possible.

**PYELOGRAPHY.** See KIDNEY, also UROGRAPHY.

**PYURIA.—ETIOLOGY.**—P Bazy and P Oudard (J d'urol. 31 321 (Apr), 581 (June) 1931) report the subject of pyuria in which all examinations for tuberculous lesions, microscopical, cultural and animal inoculations are negative. They believe the term "amicrobic" is preferable to aseptic. They divide these cases into 2 groups: (1) those which are intermittent, in which microorganisms are intermittently found in the urine, and (2) those which are continuous, in which the organisms are always absent. The intermittent disappearance of bacteria is, according to the authors, the result of an ill-defined process of autosterilization. Bazy and

Oudard also state that many cases may be of mechanical (urinary gravel and crystals), chemical or infective origin. In the last-named, the organism, passed rarely and found only after repeated examinations, is probably *B. coli* or the *staphylococcus*.

V Vintici and N N Constantinescu (J d'urol. 28 537 (Dec.) 1929) review 93 cases of pyuria, calling attention to the fact that a leukocyturia may easily be mistaken for aseptic pyuria. The differentiation is to be based on the character of the leukocytes and their grouping rather than on the number.

Pyuria, according to the authors, is the result of an inflammation of the urinary tract produced by the destruction of the white blood cells in the phagocytic struggle and in the urine itself. Other substances producing pus in the urine are salts of mercury, croton oil, ammonia, antipyrine, silver nitrate, the salts of iodine, sodium chloride and terebenthene.

Aseptic pyuria of bacterial origin is explainable on 2 bases: (1) either the rupture into the urinary passages of a closed renal or pararenal pocket containing cold pus in which the bacteria have been destroyed, or (2) a filtrable virus. The first theory is rather difficult to conceive, because living bacteria are usually to be found if frequent and numerous cultures are made, while the second theory has little support, due to the fact that pyuria is not mentioned in the description of those diseases which are attributable to a filtrable virus. In the authors' opinion, so-called aseptic pyurias of bacterial origin are false aseptic pyurias.

The question of toxins, both endogenous and exogenous, is next considered by Vintici and Constantinescu (*loc. cit.*), who believe that as soon as the bacteria

which have been the origin for the toxins are able to find their way into the urinary tract, a leukocyturia will occur and there will be a definite bacterial pyuria

V Albeck (Acta obst et gynec Scandinav 9 30, 1930) reports 226 cases of *pyuria gravidarum* in 10,000 deliveries. Sixty-nine had pyuria and fever during pregnancy or delivery, while 157 were afebrile during delivery and probably also during their pregnancy. Only 15 had a premature delivery and 6 of these cases were probably the result of intoxication during pregnancy.

In 17 of the 69 cases of pyuria gravidarum abortion occurred. Thirteen of the prematurely born infants survived, while 3 died. The infant mor-

tality was only 11.6 per cent and only 1 mother died. All of the women suffered from a persisting bacteriuria, even after prolonged medical treatment in bed.

The investigation of M. A. Griffin (Glasgow M. J. 114 21 (July) 1930) reveals that the pyurias in those cases coming to autopsy are generally the result of a pyelonephritis rather than a single pyelitis. The evidence points to a blood borne infection as the pelvis and bladder are much less affected than the kidney substance. Although the infection may be severe, the author stresses the point that it may not be promptly fatal and large areas of healing may be found. In those cases which recover he believes the only remainders are the areas of focal fibrosis.

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**RADIOACTIVE SUBSTANCES. —THERAPY.**—For years, various methods have been tried in an effort to find a satisfactory means of applying prolonged treatment to overcome the pain and functional disturbance in chronic disorders of **rheumatic origin**, and such disorders, *e g*, **rheumatic** and **gouty arthritis**, **arthritis deformans**, and **neuralgias of rheumatic origin**, have also been the subject of various methods of radioactive applications, according to G. Singer (Brit. J. Actinotherapy 5.11 (Apr) 1930). Treatments by radiation, and especially by drinking water containing radium emanation, have for a long time been accorded special attention by medical men. These treatments are all more or less prolonged. For short treatments, baths are given—those of Joachimstal and Gastein being particularly famous

on account of their high proportions of emanation. Apart from these, radioactive solutions are used by patients at home for bathing. The effect of most of these radioactive baths is not so much local, as general, *ie*, by inhalation. If local treatment of any given area be intended, preparations are available for local applications, the effects of which may be graded according to the length of time of the applications.

Many years ago, pitchblende containing radium was filled into small bags and placed on certain parts of the body, when it was desired to apply weaker concentrations of the gamma rays. The author has often seen the late Professor Neusser, in Vienna, who was associated with Mme. Curie, apply such *pitchblende bags* in cases of chronic and protracted disease, particularly of the arthritic type, and patients were told to wear

the pads containing radium constantly, so as to be always under the influence of minute quantities of radium radiation

The use of an *electrically-heated radioactive compress*, known as the "Q-ray pad" has, in almost every case, shown satisfactory results. The application of this local method, which at first was limited to the joint affections already referred to, extended to an increasing degree on account of the opportunities afforded at a large hospital. There is hardly any affection accompanied by **pain** which may not be treated by means of this compress. Success in the most serious painful disorders may occasionally be only partial, but in other cases this method of local radium treatment is remarkable for its strikingly quick results.

It is applied also to **painful abdominal disorders** of the most varied etiology, accompanied by **colic**, and to **flatulence** accompanied by spasms, to local and general **meteorisms** (which is such a troublesome symptom of quite a number of disorders in the digestive tract), to **disorders of gall-ducts, kidneys**, etc., all of which disturb the sleep of the patients. In such cases, and for refractory **sciaticas, lumbago**, etc., this compress is to be preferred to the usual thermophores and heating elements—as every chronic patient of this type (who naturally acquires an extensive experience) finds out for himself. As the result of using this compress regularly, it has been found possible to dispense with direct analgesics, it is also of great advantage, for obvious reasons, in the case of chronic sufferers. As regards the question as to why this radioactive compress proves superior to others, the writer believes it does so for 2 reasons.

1 Successful combination of local heat and radioactivity

2 Easy application, owing to the elasticity and adaptability of the compress.

For many years it has been indubitably clear to the writer that radioactivity combined with heat acts far more quickly and intensively than radioactive preparations used at ordinary temperatures. This is the reason why, for certain diseases, hot radioactive springs (e.g., Gastein) are superior to cold springs (Joachimsthal), as the author has personally noted on many occasions. As regards local effects, it appears that the radioactive effect attains its maximum owing to the action of the heat radiation on the tissues. This results not only in local analgesic effects, but in a general functional improvement of the affected tissues, due to local hyperemia.

Local hyperemia and local radiation favor absorption of the refractory rheumatic infiltrates in the muscles, tendons and joints.

The ease with which the compress can be applied to any part of the body allows a local concentration of radium emanation, heat and hyperemia at well-defined areas, thus influencing diseased areas by more intensive and speedier methods than heretofore.

**RADIUM.**—As a therapeutic agent, radium is steadily increasing in importance. Its chief field of usefulness is, of course, in the treatment of malignancy, either alone or as an adjunct to surgery. Abundant proof is at hand confirming the power of radium to control cancer throughout a wide range of its manifestations and, in many instances, to effect complete cures.

That the great majority of **cutaneous epitheliomata** are readily curable in the early stages is a well-known fact. **Cancer of the lip** is easily eradicated if diagnosed early and treated effec-

tively Radium treatment of carcinoma of the uterine cervix is thoroughly established and in leading clinics has displaced surgery as a procedure of election

As an adjunct to surgery, the judicious use of radium in competent hands will frequently add years of comfort to the patient's life Primary recurrence of the malignant growth in antrum, breast or rectum may frequently be prevented and the prognosis correspondingly improved

In hopelessly advanced and inoperable cases of cancer radium stands out as a palliative agent *par excellence* Fortunate is the patient, who, having neglected his malignancy until too late to obtain a cure, receives the benefits available at a well organized radium center or general clinic where radiotherapy is skillfully applied

An intelligent attack upon cancer demands the closest cooperation between surgeon, radiologist and pathologist The surgeon must expand his anatomical conceptions of disease to embrace the physiology of neoplasia The radiologist must no longer content himself with his knowledge of radiophysics and technic. The pathologist must clothe with life the dead cells in the microscopic field and visualize their growth and spread in the living body of the host, in order that he may judge of their response to various forms of therapy and offer a prognosis that will prove of value in determining the plan of treatment in a given case.

The utility of radium, however, is by no means confined to the treatment of malignancy Many benign disorders are cured or favorably influenced by its judicious use

Various cutaneous and subcutaneous lesions such as keloids, angiomas and birthmarks, respond well. The toxic

thyroid, the enlarged thymus, the uterine fibroid—all are proper subjects of radium therapy in selected cases The response of the leukemic patient to skillful radiation of bone-marrow and spleen is often spectacular to a degree Lymph nodes that are the seat of Hodgkin's disease, tuberculosis or nonspecific chronic inflammation are effectively attacked and subdued by radium Numerous pathological conditions usually regarded as belonging exclusively to the domain of surgery, such as enlarged tonsils, hypertrophied prostate and urethral caruncle, may be effectively handled with radium when for any reason surgical intervention is contraindicated

The literature of radium is voluminous and is growing rapidly It may be roughly classified along the following lines (1) Pure physics, (2) pure biological experimentation and research, (3) clinical application to specific problems, such as are presented by malignancy involving any particular site, tract, or type of tissue

Lack of space precludes an exhaustive survey of the progress made in the various fields of radium therapy during the past year or two Only those advances that may rightly claim the interest and attention of the general medical man or that indicate the standardization of technic in some particular field can be presented within the confines of this article

#### BREAST, CARCINOMA OF.—

I Levin (Radiology 17 1018, 1931) deplores the fact that only a small percentage of cancers of the breast are presented for examination and treatment in their early stages before lymphatic extension has occurred He states that in early cases, without axillary involvement, radical surgery gives excellent re-

sults, about 75 per cent of these patients remaining well 5 years after operation, but that if all so-called operable cases (including those with extension to the axillary and supraclavicular lymph nodes) are subjected to surgery alone, then less than 25 per cent will show successful results

He believes that the correct combination of *surgery*, *radium* and *x-ray* must be determined for each individual case, and that radiotherapy, pre- or postoperative, or both, must be added in every case of positive malignancy of the breast

A method of applying interstitial radiation to inoperable carcinoma of the breast is described by M. Cutler (Surg Gynec Obst 53 71 (July) 1931). He employs *radon needles* and applies them as if the entire breast were malignant. The needles remain *in situ* for 6 to 9 days and the total millicurie value employed at one sitting is from 100 to 130 millicuries. The needles have a value of approximately 1 millicurie per centimeter of length and are placed approximately 1 centimeter apart. No needles are inserted into the main tumor mass, only the periphery of the growth is irradiated.

Cutler states "1 Because of the radioresistance of mammary carcinoma, interstitial radiation constitutes the method of choice in the treatment of inoperable carcinoma of the breast. 2 Long radium needles that are removable permit a more uniform radiation than can be accomplished by radon seeds. 3 Adequate filtration (0.5 mm platinum) is essential in order to effect complete regression of tumors without necrosis.

"4 The irradiation of mammary carcinoma must follow the same principle as the radical operation for this disease,

*i.e.*, the entire mammary gland and lymphatic areas must be regarded as invaded regardless of the extent of the disease as previously determined by clinical examination.

"5 The peripheral or growing edge of tumor is the most dangerous part of the lesion and requires the most intense radiation. The central portion is poorly nourished, tends to bring about spontaneous necrosis, and requires relatively little radiation.

"6 Healing of ulcerated lesions of the breast can be accomplished and impending ulceration prevented by the technic of radiation that has been presented. No claim can be made, however, for the permanency of the results.

"7 Peripheral radiation by means of long removable radon needles can accomplish regression of advanced mammary carcinoma which fail to respond to other methods of radiation therapy."

Attention is called by J. M. Wainwright (Surg Gynec Obst 52 549 (Feb.) 1931) to the great frequency of involvement of the underlying muscle in carcinoma of the breast. His work with whole breast microscopic slides has demonstrated malignant deposits involving muscle in about 60 per cent of cases. He also emphasizes the occurrence of microscopic nodules remote from the parent growth in so-called operable cases, and cautions against overconfidence in interstitial radiation on this account.

The application of radiation to cancer of the breast is thoroughly discussed by B. J. Lee and G. T. Pack (Acta radiol 12 416, 1931). Their original paper should be read. Summarizing, they state

"1. Preoperative external irradiation of mammary carcinoma is of value, as proven by (a) occasional regression in

tumors so treated, (b) histological changes produced, (c) better clinical end-results. An efficient devitalizing dose cannot be delivered by external irradiation alone.

"2 To deliver an efficient dose one must use interstitial irradiation.

"3 The tissue dose delivered to the tumor by external irradiation and gold radon seeds, used interstitially, should be measured and expressed in skin erythema units. This dose should be prescribed.

"4 Tables prepared in the physical department enable the clinician to translate into terms of skin erythema units the tissue dose delivered, whether by external or interstitial irradiation (i.e., by gold radon seeds).

"5 The clinical experiments described herein have made possible the determination of the lethal dose of irradiation for carcinoma of the breast. The tissue dosage necessary to effect destruction of a radioresistant mammary cancer 3 cm. in diameter, or less, is 12 (1200 per cent) S E D. The devitalizing dose for the most radioresistant carcinoma, 3 to 6 cm. in diameter, is at least 13 (1300 per cent) S E D.

"6 The method of gold radon seed implantation is unsuitable for tumors larger than 6 cm. in diameter.

"7. The mammary gland will tolerate safely an enormous dose of interstitial irradiation.

"8 Interstitial irradiation of the axilla is a difficult practical problem. Radon implants (whether gold seeds or gold tubes) should not be placed too near the apex of the axilla, lest serious neuritis may ensue.

"9 The possible menace of dissemination of the disease by the method of interstitial irradiation has been considered. We have not seen evidence of

such dissemination in this series. Preliminary external irradiation lessens this possibility.

"10 All irradiation should be given in 3 weeks or less time.

"11 If surgery is contemplated, 6 weeks should elapse following interstitial irradiation before radical amputation.

"12 Delayed healing of the operative wound is due to 1 or more of 3 factors: (a) Excessive interstitial irradiation, (b) undue wound tension, (c) a short time interval between interstitial irradiation and surgical intervention.

"13 Eighty-six per cent of the patients in the primary operable group who were treated by interstitial irradiation and radical surgery are alive, without evidence of cancer, 1 year and 6 months after the beginning of treatment.

"14 Pulmonary fibrosis following interstitial irradiation of the breast is of infrequent occurrence and insignificant importance.

"15 The technic should not be proposed as a routine preoperative procedure. The technic of external irradiation and gold radon seeds used interstitially in measured tissue dosage, as a preoperative measure, finds justifiable usage in selected, small, well-defined carcinomas of the breast.

"16 Finally, our experience in the irradiation of mammary cancer forces the conclusion that the technic of *gold radon transfixion tubes* in the breast, axilla and paramammary regions, offers the most effective means yet devised for the destruction of mammary cancer and its accessible metastases. It should never be employed as a preoperative measure, but may well be considered as a substitute for radical surgery."

**UTERUS, TUMORS OF.**—B F Schreiner and L C Kress (Am J



Roentgenol 25 359 (Mar ) 1931) give their experience with the treatment of **cervical carcinoma** at the State Institute for the Study of Malignant Disease, at Buffalo, N Y They state that of all patients admitted, 16 per cent were suffering from this type of malignancy

From 1919 to 1925, 417 cases of cancer of the cervix were studied Of these, only 57 (13.6 per cent ) could be regarded as operable Irradiation comprised *intrauterine radium* and *external high-voltage x-rays* The original paper gives the technic followed in the treatment of this series in detail

The 417 cases were grouped as follows

"Group I—Where the lesion is confined entirely to the cervix

"Group II—Where the lesion involves the cervix extending to the vaginal mucous membrane, without definite infiltration of the broad ligament areas

"Group III—Where there is a lesion of the cervix, with or without extension to the vaginal mucous membrane, but with beginning involvement of one or both broad ligament areas, the uterus, however, being somewhat movable

"Group IV—Where the lesion originates in the cervix, with or without extension to the vaginal mucous membrane, or with distant metastases, and with fixation of the uterus

"Group V—Recurring cancer of the cervix following operation

"Irradiation in the treatment of cancer of the cervix uteri gave the following results

"Group I 62.5 per cent clinically well 5 years or more

"Group II 27.7 per cent clinically well 5 years or more

"Group III 13.2 per cent clinically well 5 years or more,

"Group IV 11 per cent clinically well 5 years or more

"Group V 6.5 per cent clinically well 5 years or more "

The technic employed in Regaud's clinic in radium therapy of **cancer of the cervix** is described by A Lacasagne (*Radiophys et radiothérapie* 2 95, 1930) This was standardized in 1923 and remains essentially unchanged Six radium tubes are utilized, 4 containing 13.33 mg ( $\frac{1}{3}$  grain) radium element apiece and 2 containing 6.66 mg ( $\frac{1}{10}$  grain) apiece The filtration is 1 millimeter of platinum plus rubber Three tubes totaling 33.32 mg ( $\frac{1}{2}$  grain) are placed in the uterine canal and 2 tubes aggregating 26.66 mg ( $\frac{2}{5}$  grain) in the vaginal fornices Another tube containing 6.66 mg ( $\frac{1}{10}$  grain) is placed centrally high up in the vagina This radium treatment lasts about 5 days in the average case

Of 350 cases treated, 20 per cent showed 5 year cures The most favorable cases showed 42 per cent alive and well after 5 years

F W Lynch (*Am J Obst and Gynec* 22 550, 1931) reviews a follow-up study of 192 cases of **cervical carcinoma**, extending over 5 to 15 years He concludes that radium treatment in this condition is greatly superior to panhysterectomy, and appends the table on following page

E Held (*Rev franç de gynéc et d'obstet* 26 373, 1931) reviews the experience with radium therapy of **cervical carcinoma** in an extensive series of cases seen at the Gynecological Clinic of Geneva from 1914 to 1930 and describes the changes and improvements effected in technic during that period During the past 5 years 86 cases have been treated with radium alone with apparent cures in 18.6 per cent

"Grade of Tumor	Cases	Treatment	Five-year Cures	
			No	Per Cent
1	14	Operation and irradiation	12	85.5
	3	Irradiation	3	100.0
2	17	Operation and irradiation	9	53.0
	9	Irradiation	1	11.0
3	71	Irradiation	8	11.3
	3	Irradiation and operation	1	33.0
4	42	Irradiation	0	0
5	43	Irradiation	4	12.1"

E Pouey (Gynecologie 30 140 (Mar.) 1931) has treated 27 cases of **cervical carcinoma** and reports 40 as apparently cured for from 3 to 7 years. He favors internal radium therapy as the method of choice, but does not hesitate to utilize other standard procedures as circumstances may require.

A statistical report is presented by G. G Ward and L K P Farrar (Surg Gynec Obst 52 556 (Feb—No 2A) 1931), covering their experience with 251 cases of **cervical cancer** treated with radium. They describe their technique, which consists of an initial dose of 2400 to 4200 mg hours, followed by meticulous post-radiation care and a monthly follow-up throughout a 5 year period. Re-radiation is employed if necessary. From their detailed tables, the following is reproduced to show 5 to 11 year results.

"Table XI—End-results of cases of **carcinoma of the cervix uteri** beyond 5 years treated only by the Ward and Farrar method, Womens Hospital—Classes I, II, III, IV

End Results.	Cases Treated	Cases Living	Percentage Living
5 years	170	44	25.9
6 years	125	29	23.2
7 years	90	19	21.1
8 years	55	11	20.0
9 years	27	7	25.9"

Their conclusions are as follows:

"1 Our experience of over 11 years with radium therapy in carcinoma of the cervix leads us to believe that the best results can be obtained with the smaller dosages of radium (2400 to 4200 mg hours) provided a frequent personal follow-up is maintained throughout the entire 5-year period, and that re-radiations are given for local recurrences in their incipency.

"2 We believe that the response to the irradiation will be more satisfactory in result, with much less morbidity, if cachexia and anemia (below 3,500,000 reds and 50 per cent hemoglobin) are combated with a preliminary fortification of the patient's resistance by a blood transfusion.

"3 We believe that the importance of postradiation care, frequent cleansing douches, outdoor air, proper nourishing diet, rest, etc., should be recognized and carried out as far as possible.

"4 We hope that future results will show that the high voltage x-ray therapy will take care of the 40 per cent gland involvement in the advanced cases, as found by Bonney. Without high voltage x-ray, our absolute cure rate of 24.7 per cent compares favorably with Bonney's 24.4 per cent.

"5 Until the combined method as advocated by Stockel, Zweifel, and others, shows better results in spite of primary

mortality, we prefer to employ irradiation *alone* in carcinoma of the cervix.

"6 We believe that in all cases in which the disease has advanced beyond the cervix, only radium and x-ray should be employed and not surgery, even though many of these patients can be operated upon successfully, because our results with radium in these advanced cases are fully equal to those salvaged by the surgery of experts and without its high primary mortality and morbidity.

"7 We believe that the results we have obtained with radium for the Class I and II cases, 57.1 per cent, without primary mortality or morbidity, are so close to the best results obtained by the Wertheim operation done by experts after years of specialized surgery in this field, that the radium method of treatment is obviously preferable to surgery in this class of case."

The plan of radiation treatment employed at the Memorial Hospital, New York, for carcinoma of the cervix is described by W. P. Healy (Radiology 14:217 (Mar.) 1930, Am. J. Roentgenol. 26:734, 1931). Irradiation for this condition was established in 1915 and since that time some 2000 cases of cervical cancer have been under observation. At present his technic comprises *x-radiation to the pelvis* and the *internal application of radium or radon*. For details the reader should consult the original article. Healy discusses the histology of carcinoma of the cervix. This is of particular interest from the standpoint of tumor response to radiation. He states: "Numerous writers have reviewed the histology of their cases of cervical cancer, and there seems to be a consensus of opinion upon certain points:

"First, the lesions are almost ex-

clusive of the squamous epidermoid variety, with a very small number of adenocarcinomata—not over 3 to 6 per cent—which arise from the cells in the cervical glands.

"Second, the squamous epidermoid variety can be readily divided into 3 large histologic groups according to variations in cellular structure and characteristics. Various names have been given to these groups by different writers, but there is no diversity of opinion on the histologic criteria of the individual groups.

"Briefly, Group I (adult, spinal type) is composed of tumors in which the predominant cell type is a fully developed, mature, adult squamous cell, with more or less tendency to pearl formation. The cells and nuclei resemble each other and have similar staining qualities. These cases comprise about 20 per cent of the total.

"Group II (plexiform, transitional, nudripe) consists of cases in which the histologic appearance is changing from that of a mature cell to one that is less mature, and the cells vary more in size and staining qualities. Mitoses are more in evidence and in the majority of cases the histologic picture suggests a pattern or architectural structure of plexiform type. This is the largest group and includes about 60 per cent of the cases.

"Group III (anaplastic, spindle, unripe, embryonal), as the various names given it imply, consists of tumors in which the histologic structure is that of a rapidly growing lesion made up of small cells, immature, with many mitoses, marked variation in staining qualities, relatively little stroma, and a tendency to invade lymphatics early. This group comprises about 20 per cent of the whole.

"These percentages vary, but always about four-fifths of the lesions (80 per cent) are in the second and third groups. It is recognized that the cell most resistant to radiation in the 3 groups is the spinal, or fully developed adult type of squamous cell—that one which typifies Group I and represents only one-fifth (20 per cent) of our total lesions. We believe it is reasonable to assume that the high proportion of relatively radio-sensitive lesions in the second and third histologic groups of cervix cancer accounts for the satisfactory response which so many of these cases make to radiation therapy, even when they are moderately advanced clinically."

Again reviewing his experience with 1574 cases of **cancer of the cervix**, W P Healy (J A M A 97 1680 (Dec 5) 1931) states his conclusions as follows

"Unfortunately a cure for carcinoma of the cervix uteri has not yet been obtained. Only from 20 to 22 per cent of all patients treated survive 5 years, regardless of the method employed. The best results are obtained by early diagnosis, followed by prompt and efficient treatment. Sixty per cent or more of the early cases may be cured for 5 or more years. Radiation therapy has not yet been stabilized and must be regarded as still in the experimental period. Marked variations in technic and principles of treatment exist in different clinics but, strange to say, the end results are quite similar. On the whole, in the treatment of cervical cancer, radiation therapy seems to have a greater field of usefulness than surgical treatment and offers more relief from symptoms and greater prolongation of life to a larger number of patients."

The modern methods of treatment of

**cervical cancer** are discussed by E Zweifel (Am J Obst and Gynec 20 595 (Nov) 1930) who concludes

"1 The methods of treatment for carcinoma of the cervix are (a) surgery, (b) irradiation, (c) surgery plus irradiation

"2 Radical total extirpation can be carried out either vaginally or abdominally

"3 Either method can be combined with irradiation

"4 Irradiation therapy may be produced by means of x-ray, radium or both.

"5 The absolute percentage of cures by (a) radical abdominal surgery is 20 per cent; (b) radical vaginal surgery is 17 per cent, (c) irradiation therapy only 17.7 per cent

"6 Irradiation may be combined with surgery as preoperative, postoperative, or pre- and postoperative irradiation

"7 It is impossible, at present, to determine which procedure is the best

"8 The combination of irradiation and surgery produces better results than surgery alone

"9 Surgery should never, therefore, be performed without irradiation

"10 The greatest advantage which irradiation possesses is the fact that it is possible to cure a certain percentage of inoperable cases

"11 Irradiation has practically no primary mortality"

An editorial in the Journal of the American Medical Association (93 923 (Sept 21) 1929) calls attention to the *dangers of excessive radiation* in the treatment of **pelvic disease** as follows:

"General emaciation and cachexia is a condition that is unfavorable to radium treatment. In such cases the method is liable to result in rapid deterioration and early death. When the red cell

count is below 3,000,000 or the hemoglobin index below 40, radium should not be applied, radium treatment has a tendency to produce a degree of anemia, probably by a systemic action on the spleen, and this in the presence of a pre-existing severe anemia may be dangerous. If hydronephrosis or pyonephrosis should be detected by the presence in either loin of a tender swelling, radium should not be applied, the resulting increased fibrosis in the broad ligaments will add to the obstruction. Rectovaginal and vesicovaginal fistulas are contraindications, as radium in such cases is apt to cause intense local irritation with sloughing. Radium should not be used in the presence of any inflammatory pelvic lesion, a foul sloughing condition of the growth is one of the most common and important of these; if radium is used before the inflammatory condition has been cleared up, the probable consequence is a massive necrosis with some toxemia and pelvic parametritis or peritonitis. In cases in which the whole pelvis is extensively infiltrated with extension from the cervical growth the use of radium even supplemented with high voltage roentgen therapy seems often to hasten rather than delay the end. Finally, radium should be withheld in the presence of impaired metabolism, especially defective excretion of nitrogenous waste products. Dr Strachan is careful to point out that some of these conditions may be overcome, and radium may then be used. One temporary contraindication which he does not mention, the condition of pregnancy, has been emphasized of late by other writers. The risk of radium to the fetus is almost, but not quite, as great as the Wertheim operation. Even so, it may at times be necessary to sacrifice the child's interest in order to treat

the mother while there is still a fair prospect of saving her life."

II. Schmitz's (Am J Roentgenol 24:47 (July) 1930) contribution on *urinary tract complications* is illuminating in this connection. He discusses the effects of the extensions of the primary cervical growth upon kidneys, ureter and bladder as well as the untoward results of radiation. In particular, he cites a case that had been treated with radium in 1915 and upon which an autopsy was performed.

He says: "The total dose applied was 3500 mg-el-hr, the amount used was 50 mg element filtered with 1.5 mm brass and 3 mm para-rubber. The radium capsule was inserted into the cervical canal 3 times for about 24 hours at each application, at an interval of 8 days. In December, 1916, the patient returned complaining of pain in the left lower abdomen and the deep muscles of the hip and a gradually increasing difficulty in evacuation of the bowels. Examination revealed a healed cervix and a hard contracted parametrium which compressed the rectum. Urinary tract disturbances were not suspected. The patient died on March 10, 1927. Postmortem examination revealed an almost total obstruction of the rectum, a total obstruction of the left ureter, with an enormous hydro-ureter nephrosis and a partial obstruction of the right ureter and kidney pelvis. Serial microscopic examination of all the pelvic tissues did not reveal any nests of carcinoma cells. The conclusions reached were (1) that the urinary tract complications resulted from scar tissue formation in the parametrium, due to progressive fibrosis from radium irradiation, and (2) that routine examinations of the urinary tract and rectum should be made before and after radium

applications and at the appearance of pelvic pains "

J O Polak (Am J Surg 6 648 (May) 1929) gives his views on the indications for radium and for operation in the treatment of **fibroids** and allied conditions. The author's rich experience in this field is reflected in this contribution which should be read in the original. From an analysis of 254 cases of **uterine fibroids**, F E Keene and R A Kimbrough, Jr (Am J Obst and Gynec 20 198 (Aug) 1930) conclude that an ideal case for radium treatment should be past 50 years of age and have a tumor not larger than a 3 months' pregnancy with profuse bleeding as the only symptom. They enumerate the usually accepted contraindications to radium therapy. In their series radium was used in 21.4 per cent of cases. They found 600 to 900 mg-hours usually sufficient.

A series of 225 cases of **uterine fibroid** seen at the Goettingen Frauenklinik from 1919 to 1925 are cited by E Wehefritz (Strahlentherapie 33 467, 1930). Of these, 68 were irradiated and 157 subjected to surgical operation. He feels that gamma radiation gives good results in cases with severe bleeding.

P Uebel (*Ibid.* 38 438, 1930) reviews 1048 cases of **fibroid** and **hemorrhagic metropathy** treated at the Wuerzburg University Frauenklinik. Of these 891 received radiation therapy, the tendency being toward the employment of intrauterine radium, which has given much satisfaction. He gives the indications for and against irradiation, as derived from this extensive series of cases.

In summarizing the results from his experience with 318 cases of **uterine myoma**, B F Schreiner (Radiology 17: 265 (Aug) 1931) states that "of these

patients, 34 were untreated and 284 were treated as follows: 90 cases were treated by the insertion of *radium* and *high voltage x-ray*, 90 were treated with *radium tubes*, 96 were treated by *external irradiation* (radium packs or high voltage x-rays), 8 cases were treated by *myomectomy* (submucous fibroids) and *irradiation*.

"Eleven cases were lost track of immediately after treatment. Nine had no bleeding symptoms.

"Of the 90 patients treated with radium and x-ray, 98.9 per cent stopped bleeding; however, 1 had a return of symptoms in 2 months and was subjected to hysterectomy elsewhere. This case might have shown better results if hysterectomy had been postponed for a few months. There was diminution in the size of the tumor in 71.4 per cent of these cases.

"Of the 90 cases treated by the insertion of radium tubes, all, or 100 per cent, stopped bleeding. Diminution in the size of the tumor was noted in 89.8 per cent of these cases.

"Of the 96 cases treated by external irradiation (radium packs or high voltage x-ray), 96.5 per cent stopped bleeding. One of these had a return of bleeding in 1 year and had to be subjected to further irradiation but has been well since. There was diminution in the size of the tumor in 75 per cent of these cases."

The cases of **cancer of the fundus** in which treatment by radium and x-ray was given at The Mayo Clinic from 1915 to 1928 inclusive, are reviewed by H H Bowing and R E Fricke (Am J Roentgenol 26 738, 1931). Summarizing, they state:

"One hundred and eighty-nine cases of carcinoma of the fundus of the uterus were referred for treatment to



the department of therapeutic radiology during the years 1916 to 1929 inclusive. The mortality was 2.11 per cent. One hundred and seventy-two (92.97 per cent) of the patients have been traced. Eighty (46.51 per cent) of these were alive at last report, 92 (53.48 per cent) have died. Four of the 92 who were operated on, and 4 who were not, died of causes other than carcinoma, such as senility, myocarditis and bronchopneumonia. Thirty-six (20.93 per cent) of the patients had lived for 5 years, and 61 (35.46 per cent) had lived for 3 years.

"Of the 189 patients, 87 were treated by operation and irradiation, and 102 were treated by irradiation only. Results were naturally better in the earlier and more favorable operable series, 31.16 per cent of the patients survived for the 5-year period and 46.75 per cent for the 3-year period. The percentages in the nonoperative series were 12.63 and 26.31 per cent respectively."

A Lacassagne (*Radiophys et radiothérapie* 2:133, 1930) discusses the results of radiation treatment in 30 cases of **cancer of the uterine corpus**. In 18 of these *radium* was placed within the uterine canal, in 6, this method was supplemented by radium applied externally; in 2 cases *x-ray* and radium were combined, and 4 cases were treated by *x-ray* alone. Of the 30 patients, 7 were improved and 5 apparently cured. Lacassagne concludes that *operation* is superior to irradiation in carcinoma of the corpus uteri.

The results of the experience obtained in the Radiumhemmet, of Stockholm, with various forms of **pelvic malignancy** are presented by J. Heyman (*Surg Gynec Obst* 50:173 (Jan—No 1 A) 1930) who states:

"Briefly summarized, our opinion re-

garding the interrelationship between surgical and radiological treatment in cancer of the female pelvic organs is as follows:

"In cases of **cancer of the cervix**, *radiological treatment* is the method of choice. *Operation* should be resorted to if radiological treatment has failed.

"Operable cases of **carcinoma of the body** should be *operated* upon and submitted to *postoperative irradiation*.

"Regarding the relatively large group of borderline cases in which surgical interference, on account of general conditions and technical difficulties, is less advisable, one must, in making the choice between surgical and radiological treatment, carefully consider the size and shape of the uterine cavity. Surgical treatment is to be preferred in cases with a large and irregular uterine cavity, whereas radiological treatment is more likely to be successful if the cavity is narrow and of regular shape.

"In cases of **cancer of the vagina**, surgery ought to be entirely replaced by *radiology*.

"In **cancer of the ovaries** an intimate cooperation between surgical and radiological treatment is required. Surgical treatment, aiming at the *removal* of the ovarian tumors, must be tried first. In patients who have had the radical operation as well as in those who have not had the radical operation, *operation* must be *followed by irradiation*. In a number of these cases radiological treatment will bring about a considerable improvement and in some it may pave the way for a subsequent successful operation."

I. de Bueben (*Ibid* 52:884 (Apr) 1931) gives his experience with the treatment of primary **vaginal cancer** during the period from 1919 to 1929 in the First Gynecological Clinic of the

Budapest University Of these cases, 28 were treated with combined *x-ray* and *radium therapy* Of these 28 patients, 9 are still living 1 after 9 years, 1 after 6 years, 1 after 4 years, 1 after 2, and 5 after less than 2 years Of these, 2 patients he considers may be regarded as cured, 1 being free from recurrence after 9 years and the other after 6 years Two lived 3 years, 1 lived 2, and 3 lived 1 year after the treatment, 12 died within the first year One did not answer repeated inquiries

**Effect on the Fetus.**—The effect of pelvic radiation received by the mother upon subsequent children was studied by D P Murphy (Am J Obst and Gynec 18 179 (Aug) 1929) He found unmistakable evidence of a deleterious action upon the fetus in cases irradiated during gestation, the most frequent result being microcephaly in the offspring He, therefore, recommends curettage as an indispensable procedure preliminary to therapeutic irradiation and also advises evacuation of the uterus if the presence of an embryo is not discovered until after radiotherapy has been given Women who had been irradiated prior to conception were found liable to give birth to unhealthy or defective children

**BLADDER, TUMORS OF.**—Tumors of the bladder are discussed by J A C Colston (Am J. Roentgenol 25 375 (Mar) 1931) as seen and treated in the Brady Urological Clinic of the Johns Hopkins Hospital All epithelial tumors of the bladder are to be regarded as potentially malignant and the possibility of growth by continuity and by implantation must be borne in mind when undertaking any form of surgical treatment Pedunculated tumors are attacked by a combination of *intra-vesical electrocoagulation* and surface

applications of *radium*, with such gratifying results that Colston believes surgery should never be employed in the usual case of this type The radium is applied by means of cystoscopic applicators, carrying 100 to 200 mgms of radium filtered through 1 mm of platinum, 800 mgm hours is the usual maximum dose for one particular course **Sessile bladder tumors** are treated along the same general lines and if the lack of proper response indicates the existence of infiltration, then the growth is regarded as an infiltrating one and a wide segmented *resection* is carried out In advanced **infiltrating tumors** surface applications of *radium* are employed together with cross-firing from the rectum and deep *x-ray* If this procedure fails, then *operation* is resorted to and the growth destroyed with the *diathermic current* The base and peripheral zone are then implanted with 1 mgm *radium needles* about 1 cm apart, the total dosage varying between 1000 and 2000 mgm hours

Colston concludes from his extensive and varied observations that the presence or absence of infiltration is the most important character of any bladder tumor and must be determined as accurately as possible before the question of treatment can be approached in an intelligent manner A careful cystoscopic examination is the most accurate method at the disposal of the physician to determine this point

He considers that **noninfiltrating tumors** are best treated by a combination of *endovesical electrotherapy* and direct *radium* application

By direct application of *radium*, **resistant tumors** can usually be made to respond promptly to the *high frequency spark* and the chances of recurrence are markedly diminished

**Infiltrating tumors** should be treated by *resection* whenever this procedure can be safely carried out, according to Colston. When, however, this is impossible, the tumor should be destroyed by *diathermy* through the open bladder and *radium seeds* implanted throughout its base.

The methods of treating **carcinoma** of the bladder at the Memorial Hospital in New York, are described by A. L. Dean and E. H. Quimby (Surg. Gynec. Obst. 53:89 (July) 1931). They believe fulguration should never be employed, as the lethal effect of the spark is deemed inadequate to destroy established cancer and stimulation of the growth may result. **Papillary carcinoma**, if its base be visible in its entirety through the cystoscope, is treated by means of *interstitial seeds implanted through the urethra*, otherwise, *suprapubic cystostomy* is performed and the *seeds introduced through this opening*. **Flat infiltrating cancer** should always be attacked through a *cystostomy*. Adequate dosage of *radon* is of the greatest importance. The danger lies in insufficient dosage. More than 50 seeds have been used in several instances totaling over 100 millicuries. Dean and Quimby estimate that 12 threshold erythema doses is approximately the maximum amount deliverable to a bladder tumor from a pelvic cycle of 4 deep therapy x-ray treatments, while the minimum tissue dose they employ when using gold implants of radon lies between 20 and 25 threshold erythemata. The superiority of interstitial radiation is thus clearly demonstrated. Summarizing, they state:

"1 We can offer hope of cure to patients to whom operation alone, short of total cystectomy, can offer nothing.

"2 Our operative mortality is less

than that from surgery alone in the proportion of 3.7 per cent compared with 10 to 20 per cent.

"3 In a series of papillary bladder cancers, between 43 per cent and 55 per cent of the patients are free from symptoms and signs of disease 3 years after treatment.

"4 In a series of infiltrating bladder cancer, between 27.8 per cent and 31.8 per cent of the patients are free from symptoms or signs of disease 3 years after treatment.

"From our experience with radium therapy as it is employed at the Memorial Hospital, we believe that an adequate dose of interstitial radiation is preferable to surgery alone in the treatment of both papillary and infiltrating types of bladder cancer, because after radium implantation the operative mortality is less and a higher percentage of patients are found free from disease 3 years after treatment."

#### RECTUM, CARCINOMA OF.—

There are 3 methods of using radium in rectal carcinoma according to J. P. Lockhart-Mummery (Brit. M. J. 1:139 (Jan. 25) 1930): (1) as a procedure supplementary to surgical excision, (2) in inoperable cancer, (3) in the place of the formal surgical attack. He employs *interstitial radiation*, but does not feel that radium should displace *surgical excision* when the latter offers a fair chance of recovery. Most of the cases treated have fallen in the inoperable group.

B. F. Schreiner and J. P. O'Brien (Am. J. Roentgenol. 25:654 (May) 1931) report 210 cases of rectal cancer. They believe that a review of statistics on this condition indicates that only 25 to 32 per cent of cases are operable. Hence about three-quarters of them require other forms of therapy. They

emphasize the necessity of early diagnosis and point out the significance of any definite change of habit in the frequency and character of the stools. The classical symptoms of advanced rectal cancer should not be forgotten.

J. Ewing's ("Neoplastic Diseases," W. B. Saunders Co., Philadelphia, 1928) grouping of carcinomata of the rectum from the standpoint of pathology includes (1) adenocarcinoma destruens, (2) stenosing fibrocarcinoma, (3) gelatinous adenocarcinoma; (4) papillary carcinoma, (5) multiple carcinoma following polyposis; (6) epithelioma, (7) melanoma.

Schreiner and O'Brien (*loc. cit.*) have developed their technic of radiation until at the present time they treat all cases with *gold emanation seeds* together with *external packs* or heavily filtered high voltage *x-rays*. This they believe to be far superior to other methods. They group their cases as follows:

"Group 1. All cases in which the disease was local and confined to the wall of the rectum or anal canal and was fairly movable.

"Group 2. All cases in which the disease had infiltrated the surrounding tissues and was fixed—mechanically inoperable.

"Group 3. All cases with widespread metastases in the liver, mesenteric nodes, lymph nodes or groins."

The results of their treatment are as follows:

"1. In Group 1 cases, 17 per cent. have been well 5 years or more.

"2. In Group 2 cases, which were hopelessly inoperable, 2 cases, or 14 per cent., are well 5 years or more. Three cases have survived for 5 years or more. Of all of the Group 2 cases, 39 per cent. have had palliations of from 1 to 4 years.

"3. All the cases in group 3, those with disseminated metastases, died. Only a few of these had palliation."

Studies upon 303 cases of rectal carcinoma have been reported by E. P. Hayden and W. M. Shedden (*Surg. Gynec. Obst.* 51:783 (Dec.) 1930). They review the accepted methods of treatment by radiation as practiced in leading clinics in this country and abroad and, after a thorough analysis of their own very considerable series, present the following summary:

"1. This series embraces 303 cases of clinically diagnosed cancer, observed between 1912 and 1928.

"2. Adenomatous polyps constitute the most dangerous precancerous lesion.

"3. The fifth decade of life shows greatest incidence of cases.

"4. Family history of cancer is obtained in only 7 per cent. of the cases.

"5. Malignant adenoma and adenocarcinoma grade 1, the 2 lowest grades of malignancy, form 77 per cent. of the 101 cases available for grading.

"6. Biopsy for diagnosis, prior to instituting therapy, is always advisable and never harmful.

"7. Change in bowel habits, bleeding, and rectal pain should always suggest the possibility of cancer even though hemorrhoids also are visible.

"8. Digital rectal examination is sufficient to make a diagnosis in 95 per cent. of cases.

"9. Every cancer of the rectum is operable if discovered early enough, and the period during which it remains operable is longer than in most other cancers.

"10. Obstruction necessitating emergency colostomy is rare in rectal cancer.

"11. Colostomy, as an adjunct to radical operation, is always necessary.

"12. In the entire series only 21 cases who had positive pathological reports of

cancer are alive without symptoms, and *all* have had complete operations

"13 A radical resection, by one of several methods, and including colostomy, offers the patient his best and, we believe practically his only, chance of cure

"14. Radical operation definitely prolonged the life of 42 who subsequently died of recurrence

"15. Radium and x-ray, as at present used, must be considered purely as palliative agents in the treatment of cancer of the rectum

"16 Our patients receiving no treatment lived about the same length of time, on the average, as did those radiated as described. Changes in technic of application may, in the future, improve this situation

"17 Surgical diathermy is of use in reducing the bulk of an inoperable growth "

**BONE, TUMORS OF.**—The technic and results of radiation treatment of osteogenic sarcoma are discussed by G E Pfahler and L D Parry (Am J Roentgenol 25 761 (June) 1931). They believe heavy *radium packs* to be superior to x-ray and on the basis of 58 cases treated by irradiation conclude that radiotherapy gives results at least as good as, if not better than, those obtained by surgery alone

W Magnusson (Acta Radiol 12. 101, 1931) presents the results obtained in 39 cases of bone sarcoma treated at Radiumhemmet, Stockholm, from 1910 to 1928. Radiotherapy was confined, in the main, to inoperable cases and cases already operated upon.

"In no instance was permanent healing obtained by radiological treatment alone (16 cases)

"In 1 case of osteogenic sarcoma, which had been operated on, but not

radically, healing lasting more than 3 years was obtained

"Of the cases operated on and treated radiologically, 3 are alive with no symptoms after 7 years or more. In 2 of these, the sarcoma was of the osteogenic type, and 1 Ewing's sarcoma

"With regard to the indications for radiological treatment he emphasizes the fact that a distinction should be made between osteogenic and Ewing's sarcoma

"The results of radiological treatment in osteogenic sarcoma so far do not justify the relinquishment of surgery as a means of dealing with these tumors. In operable cases, a combination of radiological and surgical treatment should be adopted. Inoperable cases should be treated radiologically. Even in cases in which the growth has become generalized, a good palliative effect can sometimes be obtained

"The radiosensitivity of Ewing's sarcoma is pointed out. For this type of growth exclusive radiological treatment may be regarded as justified

"As to the technic, close application of radium is advised against. Whether telerradium treatment should be preferred to roentgen cannot, as yet, be determined. Large doses—from 1 to 15 erythema dose, focally—are regarded as necessary. High filtration and large focal distance are imperative. It is considered best to give the largest possible dose in the first series of the treatment, while the growth is most sensitive and the surrounding tissues, as yet, uninfluenced

"In dealing with Ewing's sarcoma, distribution of the dose over a rather long period is advisable.

"Coley's toxin treatment may be employed alongside of the radiological treatment "

**CARCINOMA OF UPPER RESPIRATORY TRACT.**—The treatment of malignancy in the **sinuses** and **nasopharynx** is discussed by D. Quick (Radiology 14 191 (Mar) 1930). He calls attention to the wide range of tumor type that may be encountered in these regions, as a result of the complex embryology of the parts. Ewing has enumerated 37 varieties of neoplasm to be found in or about the nasal passages. Quick emphasizes the pronounced frequency of antral involvement. Of 136 malignant tumors of the antrum examined in his service between 1917 and 1929, 83 per cent were found to be too far advanced to be amenable to radical excision of the superior maxilla. Anatomical difficulties offer equal opposition to effective surgery and to adequate irradiation. A combination of these procedures is usually indicated and may offer reasonable hope of success. The intensity of radiation required for the eradication of the more adult types of epithelial tumors has been worked out by Martin and Qumby and found to be between 7 and 10 erythemas. This demonstrates the great importance of delivering a sufficient quantity of a proper type of radiation to the tumor-bearing area. *Radon* implants are employed at the primary site, and high voltage *x-rays* directed to the neck in cases with metastasis. *Radium packs* and *radium emanation* may also be used in connection with surgical dissection in cases of **epidermoid carcinoma**.

Quick reaches the following conclusions:

"1 Surgical exploration of the paranasal sinuses and biopsy should be resorted to earlier and more frequently, so that earlier diagnosis of new growths may be made

"2 With a few exceptions, the prin-

ciples applying to surgical removal of cancer in general cannot be carried out in dealing with growths in the paranasal sinuses

"3 Radium and x-rays are of value in treating this group of cases, but, except in palliative procedures, must be used in conjunction with surgery

"4 Radium and x-ray may be depended upon to eradicate the tumor tissue if applied accurately and uniformly throughout the growth in sufficient dosage

"5 Surgery must be employed to provide exposure for radium application and adequate drainage

"6 The anatomical relations of the parts are such that infection is a much greater menace here than in new growths in most other locations"

G. S. Sharp (*Ibid* 17 984, 1931), also writing from the Memorial Hospital, details the technic of dealing with **antral malignancy** and presents the following summary

"Radium and x-radiation must be depended upon to deliver a lethal dose to the tumor

"The minimum lethal dose is standardized for carcinoma, with and without bone invasion of the antral walls

"Preliminary surgical exposure of the contents of the antrum must be sufficiently wide to permit the accurate and uniform placement of radon implants throughout the tumor-bearing area

"Carcinomatous involvement of the floor of the orbit requires the exenteration of the contents of the orbit in addition to an intraoral antrotomy for an adequate approach to this type of growth extension

"The cautery removal of the bulk of tumor tissue shortens the convalescent period by providing free drainage. This procedure has assured in many patients



a recovery which otherwise would have been doubtful

' Closure of the aperture in the floor of the antrum by mechanical means is effective and comfortable for the patient. Later plastic closure is probably ill-advised in patients recovering from carcinoma of the antrum "

#### **MOUTH, CARCINOMA OF.—**

G E Pfahler and J H Vastine (J A M A 96 664 (Feb 28) 1931) relate their experiences with the use of pure gamma radiation in the treatment of intraoral malignancy. Believing that most mouth cancers develop upon pre-existing benign lesions, particularly leukoplakia, these authors emphasize the wisdom of treating all such conditions with care and promptness.

In attacking carcinoma they follow the biologic principles of irradiation laid down by Regaud and employ heavily filtered radium both within the mouth and transcutaneously as follows:

For surface applications, the radium element is screened with the equivalent of 3 or 4 mm of lead and maintained at a distance of 4 cm from the skin by means of a mold. Usually from 150 to 200 mgm is applied to the side involved and 50 to 100 mgm to the opposite side. From 20,000 to 50,000 mgm hours of radium element irradiation is commonly employed. It has been found that with this technic 24,000 mgm hours can be given within 2 weeks and, as a rule, 36,000 mgm hours within 3 or 4 weeks. A deep erythema of the skin develops and is maintained. The epidermis subsequently desquamates. From 1000 to 3000 mgm hours of intraoral radiation, screened by 1 to 2 mm of platinum, are added, being given between the periods when the external packs are in use.

Pfahler and Vastine emphasize the necessity of individualizing the patients and of avoiding an inflexible routine. They have treated 111 patients by this method, 39 remaining symptom-free and apparently well after from 1 to 5 years. Treatment was stopped in 4 patients, 5 could not be traced and 44 have died. The authors believe that one-half of intraoral cancers should prove curable if the patients receive the benefits of this method of treatment as soon as they come under medical care. They tabulate the *advantages* of pure gamma ray irradiation as follows:

"1 It is painless at the time of application, though it causes soreness and swelling in the mouth at the height of the radiation effect.

"2 It does not require an anesthetic.

"3 It does not require hospitalization.

"4 It does not produce mutilation.

"5 It usually does not produce constitutional symptoms.

"6 The skin effects, when carefully managed as directed, are of no consequence.

"7 In tongue cases, the function of the tongue is preserved.

"8 It usually causes the disappearance of metastatic lymph nodes. When these are sluggish, we sometimes insert radium needles into the lymph node. If the glands break down they are removed surgically."

"The *disadvantages* of pure gamma radiation treatment are as follows:

"1 It is exceedingly expensive, because one is only using a small portion of the total radiation.

"2 It is not very practical to hire radium because one must pay while it is in transit.

"3 A considerable quantity of radium must be available if one is treating a number of patients, and any one who

treats only a few patients generally lacks experience

"4 It interferes with the occupation of the patient during a period of at least a month

"5 It requires the constant or daily supervision of the experienced radiologist and cannot be turned over to technicians

"6 It requires the constant cooperation of the patient, which may be difficult to obtain

"7 The prolonged treatment that is necessary may be interrupted by ignorant patients who do not appreciate the seriousness of the disease or who consider themselves well prematurely

"8 The greatest possible precautions against undue personal exposure must be taken by the radiologist and the technician because of the large amounts of radium that must be used "

In his contribution on the therapy of cancer of the mouth, C. C. Simmons (Am. J Roentgenol 26 5 (July) 1931) reports his experiences drawn chiefly from the Collis P Huntington and Massachusetts General Hospitals and based upon a study of 763 cases during the period 1918-24. He stresses the importance of certain predisposing pathological conditions of the mouth and certain etiological factors such as tobacco and poorly fitting dental appliances. He notes the occurrence of leukoplakia in over 20 per cent of the cases and a positive Wassermann reaction in 18.7 per cent of 411 patients to whom this test was applied. With regard to radiation treatment, he employs *gold seeds* for the local growth and *high voltage x-rays* for the glands of the neck. Occasionally *gamma radiation* is used externally, the patient receiving approximately 32,000 mch at 10 cm with 2 mm of lead filtration through 2 portals.

Summarizing, he states

"It is impossible to lay down any fixed rules for the treatment of oral cancer. Each case must be considered separately and the appropriate line of procedure determined upon after all of the factors that influence the prognosis have been considered. It is also important to determine at the outset whether the treatment is given with the hope of permanent cure or as a palliative measure

"The local growth can be destroyed either by radiation or by operation, but surgery is to be preferred in the treatment of early cases or cases in which bone is involved

"If the rules advocated by the American College of Surgeons are employed in reporting the results of treatment of cases of oral cancer, it is seen that in suitable cases more cures result by surgical removal than by radiation treatment

"If the growth is highly malignant and of any appreciable size, radium treatment is to be advised even if there are no palpable glands in the neck, as this group is radiosensitive and the possibility of surgical cure is remote

"There is also a certain group of cases with considerable infiltration of the floor of the mouth that respond better to radium treatment than to surgical excision

"In the treatment of the local growth by radium, gold seeds of emanation have been employed

"The prognosis depends more on the situation of the tumor and the degree of malignancy as determined by pathological examination, than on any other one factor

"The absence of small palpable glands in the neck does not necessarily mean that the lymphatics are not involved. On the other hand, palpable glands are

in many instances hyperplastic and are not necessarily diseased

' Surgery is employed in suitable cases in treatment of the glands of the neck, but much harm may be done by operation if the glands are extensively involved

"In the cases with obvious metastatic glands in the neck, the lymphatics are treated by high voltage x-ray supplemented in certain instances by seeds of

The underlying principles are those set forth by Regaud and applied by him at the Radium Institute of the University of Paris. Widmann's contribution should be read by all interested in this type of radiation technic

O. N. Meland (*Ibid* 26:20 (July) 1931) analyzes 520 cases of intraoral malignancy studied at the Soiland Clinic from 1924 to 1930 and presents the following tabulation

	Lip	Cheek and Alveolus	Tongue and Floor of Mouth	Tonsil and Larynx	Total
Nodes at first examination	22	25	36	36	119
No nodes at any time	248	54	48	14	364
Developed glands while under treatment	15	2	7	4	28
Recurrent postoperative nodes	3	1	5	0	9
Totals	288	82	96	54	520

radium emanation. Permanent cure is not to be expected but life is considerably prolonged by treatment

"Radiation treatment has not been used as a prophylactic after radical neck dissection, as in the small group of cases available for study it apparently did not affect the percentage of cures, in comparing them with a similar group of cases not treated. In cases of recurrence after operation, however, life was considerably prolonged by treatment."

B. P. Widmann (*Ibid* 26:12 (July) 1931) describes his technic in the treatment of cancer of the mouth. He utilizes "surface" or "contact" applicators of radium in attacking the primary lesion and radium packs and x-ray to the sides of the neck. He advocates heavy filtration and proportionately heavy mgm. hours dosage, 50,000 to 60,000 mgm. hours have been given to both sides of the neck within 2 months

In regard to cervical gland involvement, he divides his cases into 3 groups: (1) Those with no clinical evidence of malignancy in the lymph nodes receiving drainage from the malignant area, (2) patients with one or more surgically removable unilateral nodes, (3) cases presenting advanced unilateral or bilateral involvement. In the first group he employs *high voltage x-ray* or, occasionally a *radium pack* with 1 mm. brass and 3 cm. distance. In the second group a thorough course of *x-ray* is given covering a period of 3 to 4 weeks. If this fails to effect an improvement, *radium packs* are applied or resort is had to *electrosurgery*. Occasionally, for deep involvement, *block dissection* is performed. In the third group palliative therapy with suberythema doses of *x-ray* and *radium* is carried out.

The technic employed at the Memorial Hospital in New York for the radiation

therapy of cancer of the mouth is given in detail by H. E. Martin and G. S. Sharp (*Ibid* 26 28 (July) 1931). Reliance is placed upon the interstitial gold radon seed developed by G. Failla (*Am J Roentgenol* 16 507 (Dec) 1926) in 1925, and since that time over 2000 interstitial applications have been made in the intraoral department. The routine treatment of mouth malignancy calls for *radon implants* combined with *external radiation*. They defend the use of permanent implants and answer the usual objections to allowing foreign bodies to remain in the tissues by referring to their repeated experiences with cases where the implants gave rise to no symptoms whatever and where the patients were not aware of their presence.

Cervical metastasis is treated by interstitial radiation of the separate nodes by gold seeds. This procedure is felt to be superior to the surgical block dissection of the neck.

For radiotherapists not in a position to employ gold radon implants, Martin and Sharp recommend the use of very small *radium element needles*, say 1 to 5 mgm each.

Nine cases of *epulis* were treated by A. Soiland and W. E. Costolow (*Ibid* 23 639 (June) 1930) with *radium element* or *radon*. All of these have shown a clinical cure and have remained well for more than 2½ years. They believe radium to be specific in the destruction of *epulis* and claim that successful results are obtainable with dosages that will not damage the teeth or gums.

**REFRACTION.—CYCLOPLEGICS.**—A. D. Prangen (*Am J Ophth* 14 665 (July) 1931) advocates a more intelligent and scientific use of cycloplegics. After cycloplegia the

residual accommodation should be determined. The near vision should be indistinct and a +3.00 diopter lens placed in front of the eye should enable the patient to see fine print. The near point and the far point, measured in centimeters, are divided into 100, to give the values in diopters. The equation, amplitude equals near point minus far point, gives the amplitude of accommodation which should always be determined in order to obtain accurate data as to the effect of a drug on accommodation. Prangen found the residual accommodation after a cycloplegic to be from 2 to 3 diopters, while Duane considered it to be less than 1 diopter.

The procedure employed by Dorland Smith (*Am J Ophth* 14 498 (June) 1931) for estimation of total refractive error without a cycloplegic is as follows. The correcting astigmatic lens, determined by the ophthalmometer, is placed before each eye and a rapid retinoscopy is done. Spherical lenses sufficiently strong to blur each eye beyond  $20/200$  are then added. Minus lenses are then added before each eye at the same time, until vision reaches  $20/200$ . This completes the cycloclamic test. This correction, less 1.5 diopter sphere, should give  $20/20$  vision in each eye. With this as a guide, the exact correction to be ordered is determined by whatever method the examiner prefers. The underlying principles of cycloclamia are: (1) that the usual mathematical difference of correcting lens between  $20/200$  and  $20/20$  is 1.50 diopter sphere, (2) greater relaxation is obtained when both eyes are blurred than when sharp vision is permitted.

**LENSES.**—The prescribing of *tinted lenses* for apparently healthy eyes is deprecated by L. M. Fink (Minnesota

Med 13 632 (Sept ) 1930) because he finds that from 15 to 35 per cent of the visible rays, which stimulate the retina into activity, are cut down by them. More attention should be given to illumination and hygienic measures in order to avoid glare. A tinted lens may be prescribed in a myope, to cut down the sharpness of an image, or in physical diseases and neurasthenia in which the general function of the eye is often impaired.

Experiments with *contact lenses* in the last 100 years have failed, according to L. Heine (Lancet 1 631 (Mar. 21) 1931), because a fixed scleral radius of 12 mm has been employed and no attention has been given to the application of the glass to the cornea. The writer states that a glass which is relatively flat compared with the natural corneal curve must lie on the middle of the cornea, while a glass that is more highly curved than the natural cornea must touch it with equal pressure around its circumference. He recommends the use of a rubber sucker (not the finger-nail or ivory spatula) for insertion and removal of the lens, to avoid damage to the edge of the glass.

**MYOPIA.—*Etiology.***—De Wayne Hallett (Am J Ophth 14 143 (Feb ) 1931) believes that myopia is caused by paranasal sinusitis which, by localization of toxins or organisms in the eye, produces a posterior sclerochoroiditis, thus weakening the tissues and permitting them to stretch. He mentions the opinion of Newman, who believes that heredity, prenatal and postnatal malnutrition, and too much close work cause an interference with the nutrition of the internal elastic membrane of the eye and that, once the elastic tissue is stretched, it is unable to withstand normal intraocular pressure and stretches

still more. For juvenile myopia he recommends **atropine** instilled into the eye daily for a period of 2 months.

**Treatment.**—Further experience has confirmed the previous impression of Meyer Wiener (Am J Ophth 14 520 (June) 1931) that persistent use of **epinephrin solution** in the eyes and **physical exercise** tend to inhibit the progressive development of certain types of myopia.

In his experiments with anesthetized dogs, L. L. Mayer (Am J Ophth 14: 908 (Sept ) 1931) found that **epinephrin** 1 1000 and 1 100 in 3 minim (0.18 c.c.) doses in the conjunctival sac and subconjunctivally have no effect on the pulse rate or blood-pressure. Clinical investigation of 10 patients receiving this dosage in the conjunctival sac showed similar negative systemic effects. The writer concludes from both animal and clinical investigation that epinephrin 1 1000 solution or 1 100 has no effect on the general blood-pressure or pulse rate when used as eye drops, and that epinephrin 1:100 instilled in the conjunctival sac of young people with myopia is a harmless procedure.

In a series of 154 myopic patients constantly wearing **full correction** reported by Edward Jackson (Am J. Ophth. 14:719 (Aug.) 1931), 45 per cent of the eyes showed no increase of myopia; 34 per cent showed an increase of less than 1 diopter, and only 21 per cent showed an increase of 1 to 2 diopters. He recommends avoidance of much use of the eyes for near vision in early childhood, constant wearing of accurate correcting lenses, outdoor living and exercise, and attention to general health and nutrition.

**RETINOSCOPY.**—G. H. Stine (Am. J Ophth 13:101 (Feb.) 1930) reports variation of as much as 7

diopeters in the skiascopic findings of the visual and extravisual pupillary zones in his series of 277 normal cases. He states that the lens is the most important factor in producing these aberrations.

### RETINA.—ANGIOMATOSIS.

—Three cases of angiomatosis retinae are reported by A. J. Bedell (*Am J Ophth* 14:389 (May) 1931), who mentions the following points of interest in this condition: (a) the family history, (b) the dilatation of 1 or more veins and the whip-lash arteries, (c) the color of the vessels, (d) vascular angiomata; (e) detachment of the retina; (f) vitreous opacities, and (g) secondary glaucoma.

**ARTERIOSCLEROSIS.—Classification.**—The retinal changes found in arterial hypertension, are divided by A. M. Fishberg and B. S. Oppenheimer (*Arch Int Med* 46:901 (Dec) 1930) into 3 classes: (a) Retinal arteriosclerosis and arteriosclerotic retinopathy. Retinal changes which occur with or without hemorrhages and punctate exudates, but without cotton-wool patches or edema of the disc, are significant purely of arteriosclerosis. (b) Malignant hypertensive neuroretinitis, characterized by edema of the disc, marked narrowing of the arteries, and cotton-wool patches and hemorrhages in the retina, occurs in glomerulonephritis, essential hypertension and in toxemia of pregnancy. The prognosis is poor. (c) Choked disc due to increased intracranial pressure and edema of the brain is seen in glomerulonephritis but not in essential hypertension. Prognosis is not necessarily bad.

**Etiology.**—In a discussion of sclerosis of the retinal arterioles, H. P. Wagener (*Arch Ophth* 3:335 (Mar) 1930) points out that these changes

affect vision only when they become sufficiently advanced to interfere with the nutrition of the retina or when they are complicated by edema, hemorrhage, aneurism, spasm, thrombosis of the retinal vein, or arteriosclerotic retinitis.

Moore believes that the retinitis of arteriosclerosis is due to a local arterial disease and not to renal factors. In addition to sclerosis of the retinal arteries the condition is characterized by the presence of hemorrhages and bright white dots of exudate without surrounding edema.

### DEGENERATION, CYSTIC.—

Cystic degeneration of the retina may be found in practically every pathological eye condition, according to B. Samuels (*Arch Ophth* 4:476 (Oct) 1930), and is due to disturbances of circulation caused by papilledema, glaucoma, obstruction of the central vein or toxins. Cystic formation is caused by simple death of the cells without distention, or by pressure atrophy with distention. Recently formed cysts contain albuminous fluid, old cysts are filled with clear fluid. He classifies the cavities according to the ocular lesions in which they occur: (1) detachment of the retina, (2) glaucoma, (3) disease of the blood vessels, (4) papilledema, (5) iridocyclitis, (6) endophthalmitis; (7) choroidal tumors.

### DETACHMENT.—Etiology.—

According to J. Lijó Pavia (*Rev oto-neuro-oftal* 6:147, 1931), detachment of the retina may be caused by: (a) diseases of the nose and sinuses, (b) infections such as syphilis, tuberculosis and rheumatism, (c) diathesis, (d) endocrine disturbances and (e) heart or kidney disease. He reports a case in which septic pyemia caused changes in the pigment epithelium followed by uveal tract involvement. A case of detachment of the retina is also reported.



in which he describes his method of locating and recording the site of the tear by the aid of stereoscopic photographs

A J Bedell (Am J Ophth 13 390 (May) 1930) reports the case of a patient who was struck in the eye by a fist. A large vitreous hemorrhage, rupture of the choroid, and detachment of the lower  $\frac{1}{3}$  of the retina were observed. Six weeks later the hemorrhages had become absorbed, the retina had returned to its normal position, and vision was then 20/15.

**Treatment.**—**Ignipuncture** was performed by G S Derby (New England Ophth. Soc (Jan 20) 1931, Am J Ophth. 14 1049 (Oct) 1931) in a case of detached retina in which vision was 4/200. After 10 days in bed, although the hole had not been struck, the retina was flat and vision was 20/40. Greenwood is of the opinion that far better results are obtained by ignipuncture than by any older method.

J. Meller ("Augenärztliche Eingriffe, ein kurzes Handbuch für angehende Augenärzte," 3d Edit, Verlag von Julius Springer, Vienna, 1931), advocates **ignipuncture** for retinal detachment. He believes that tears and holes are very common in fresh detachments and that the more recent the retinal detachment is, the more frequently these can be demonstrated. He states that they are definitely visible in two-thirds of the cases and present in even more, although often overlooked because of their location or small size.

In 3 cases of detached retina, A. L. Brown (Am J Ophth 14 429 (May) 1931) performed the **Gonin cautery puncture**. In 2 of these cases the results were most encouraging, visual acuity and fields were restored to normal. The importance of completely

closing a retinal tear by means of the cautery is emphasized.

F H. Verhoeff (New England Ophth Soc (Jan 20) 1931, Am J Ophth 14 1049 (Oct) 1931) recommends **cautery puncture** and reports good results in 2 cases of detached retina treated by this method.

J H Doggart and C D Shapland (Brit J Ophth. 15 257 (May) 1931) performed the **Gonin operation** for retinal detachment on 75 patients and report the following results. Twenty-four were discharged with reattachment of the retina and full visual field, 12 showed improvement in visual acuity or in the visual field, and the remaining 39 were unchanged or worse. In other words, they obtained 32 per cent of cures and 16 per cent of improvements in a condition which had previously been considered almost hopeless.

Gonin reports a larger number of successes from his method of **ignipuncture** than from any other procedure. He finds that holes occur most frequently in the periphery of the retina between the equator and the ora serrata, especially in the superior temporal quadrant. The prognosis is most favorable when the detachment is of only a few weeks' duration. A series of 30 cases of this recent type of detachment has yielded successful results in 70 per cent, while in cases of 1 to 3 months' duration, 50 per cent were successful.

In order to prevent the formation of a fistulous opening caused by necrosis of the wound margin, C E Finlay (Arch. Ophth 4 662 (Nov) 1930) has modified **Gonin's surgical method** for the treatment of retinal detachment. His procedure is as follows. The conjunctiva and Tenon's capsule are incised down to the sclera and a series of longitudinal cuts is made in the sclera, until

retinal fluid exudes. The scleral surface is then cauterized superficially about 0.5 mm from the edges of the wound and the conjunctiva closed with sutures.

**LIPEMIA.**—In addition to a review of 36 cases previously reported in the literature, W. R. Parker and A. M. Culler (Am J Ophth 13: 573 (July) 1930) describe 2 cases of lipemia retinalis. From their study of these cases they conclude that

(a) Diabetes is the only disease in which lipemia of the retina occurs in sufficient degree to be recognizable ophthalmoscopically.

(b) Lipemia retinalis occurs most frequently in young diabetics because their fat metabolism is less efficient than that of older people.

(c) Diabetics do not present lipemia retinalis unless there is acidosis.

(d) Lipemia appears when blood fats fall below 2.5 per cent.

(e) The prognosis in diabetics does not depend on the presence or absence of lipemia retinalis.

**TUMORS.—Etiology.**—W. L. Benedict (Arch Ophth 2: 545 (Nov) 1929) reports the occurrence of *retinoblastoma* in twin girls, 1 of whom had a growth in the left eye and the other a growth in each eye. Because of the similar location of the tumors in the left eye of each girl, he reasons that these tumors develop from fetal rests which originate from the single ovum from which these twins developed.

**Differential Diagnosis.**—Ralph I. Lloyd (Am J. Ophth 14: 27 (Jan) 1931) discusses a group of conditions which may simulate and be confused with *retinoblastoma*, in the first 3 years of life, *i e*, within the age limit of *retinoblastoma*. These conditions are grouped as *pseudoglioma* and include remains of the vascular tunic of the lens, retinal de-

tachment, cyclitic membrane, tuberculous choroiditis and uveitis, metastatic inflammation, and a rare condition called Coats's disease. The first important sign of true glioma is the presence of a peculiar colored mass in the vitreous with vessels running over it. A true glioma rarely, if ever, exists in an eye the pupil of which reacts normally.

A case is reported by M. Cohen (Arch Ophth 4: 368 (Sept) 1930) of a 3-months-old child who showed typical manifestations leading to the clinical diagnosis of *retinoblastoma*, but the microscopical diagnosis was plastic cyclitis with sequelæ. Hemorrhages in the aqueous, necrosis and iridocyclitis, due either to the liberation of toxins or to the local recurrence of the growth, are suggestive features in making a diagnosis of *retinoblastoma*.

**RETROPHARYNGEAL ABSCESS.—ETIOLOGY.**—Retropharyngeal abscess is usually due to adenoiditis, rhinitis, sinusitis, otitis, or may result from an infection of the upper cervical vertebræ, as seen in Pott's disease. At times it follows trauma due to a foreign body, such as a fish-bone that lodges in the posterior pharyngeal wall. Retropharyngeal abscess is a disease of childhood, being most frequent between the ages of 2 months and 4 years and during the cold months of the year, when the respiratory infections are prevalent.

**SYMPTOMS AND DIAGNOSIS.**—According to H. M. Greenwald and C. R. Messeloff (Am J M Sc 177: 767 (June) 1929), who review 59 cases, an average of 10 days elapsed between the appearance of the first symptom and the time of diagnosis. The earliest symptom in their series was either restlessness, fever or an enlarged cervical

gland The enlarged gland is usually situated at the angle of the jaw at the anterior border of the sternocleidomastoid muscle The presence of an enlarged gland in these regions should always lead to the suspicion of a retropharyngeal abscess and should be excluded, if possible, by the only absolute method of diagnosis, *viz*, palpation of the throat Difficulty in swallowing, change in the character of the voice, respiratory difficulty and torticollis are characteristic symptoms Frequently, inspection reveals nothing and digital examination must be resorted to, which must be done with great care Rough digital examination may rupture an abscess and suffocate a patient In the above authors' series the mortality was 73 per cent

**COMPLICATIONS.**—The common complications are (1) spontaneous rupture of the abscess causing asphyxia, (2) burrowing of the pus inwardly, dissecting the tissues laterally to the side of the neck behind the large vessels and the sternocleidomastoid muscle, and appearing at the posterior triangle of the neck, (3) extension of the pus downward along the prevertebral fascia into the lower part of the neck; (4) extension of the pus behind the esophagus into the posterior mediastinum A relatively infrequent and serious complication is erosion of one of the main blood vessels in the vicinity of the abscess The vessels most likely to be involved are the internal carotid artery and, to a lesser extent, the internal jugular vein and the vertebral artery

**TREATMENT.**—The treatment in the stage of nonsuppurative lymphadenitis is medical, operative procedure being contraindicated in this stage. As soon as fluctuation is present, the mass should be incised and aspirated if pos-

sible In opening the abscess, the head should be lower than the shoulders, so that drainage of the pus will be away from the larynx

**RHEUMATIC HEART DISEASE.** See CARDIOVASCULAR SYSTEM

**RHEUMATIC PERITONITIS.**—That rheumatic fever is not merely an acute arthritis, but a more generalized disease process, is becoming more and more commonly understood F. C. Wood and E. L. Eliason (Am J M Sc. 181 482 (Apr) 1931) report a case of a 13-year-old patient, with a past rheumatic history and a definite cardiac lesion, who developed lower abdominal pain, diarrhea and signs of peritoneal irritation The patient was operated upon on the supposition that a ruptured appendix and pelvic peritonitis were present. Operation disclosed no suppurative focus, revealing merely an acute serositis and subserositis, with an abundance of fluid in the peritoneal cavity. Within a few days after operation the abdominal signs and symptoms largely subsided, but the fever and general phenomena persisted Nine days after operation acute pericarditis developed, and after a severe course of typical cardiac rheumatism of 6 weeks' duration the patient died The authors consider this a case of "rheumatic peritonitis," which condition has been discussed in the literature by various clinicians.

**ROENTGEN RAYS.** See X-RAYS.

**RUBELLA (GERMAN MEASLES).**—Rubella occurs in distinct epidemics and has rather marked seasonal variations M. O. Belson (New England J Med 203 1076 (Nov. 27) 1930) described one such epidemic, con-

sisting of 118 patients in the vicinity of Boston, from January to June, 1930. The symptoms were typical in every respect to the text-book descriptions. The average age of the patients was 4.5 years. Sixty per cent of the patients had no fever, complications were very rare and no deaths occurred. L. O. Finkelstein and R. W. Stojanowskaja (Arch f Kinderh 90 181 (May 24) 1930) observed an epidemic of the disease occurring in 28 children in a tuberculosis sanatorium. The symptoms were typical in every respect except that the lymph gland enlargement was not present in any instance. The writers were at first inclined to consider the disease as one of the more rare contagious exanthemata, but the other symptoms were so characteristic of rubella that they finally classified it as an atypical form of that disease.

A rare complication of rubella was observed by J. H. E. Brock (Lancet 2 1190 (Dec 7) 1929). A patient with a typical attack developed a headache, fever and divergent strabismus on the third day of his illness. The spinal fluid contained 296 cells, there was an increase in the protein of the fluid, an

absence of microorganisms on culture, and a negative Wassermann test. Within 6 or 7 days the patient improved and made an uneventful recovery. The condition was diagnosed by the writer as a *meningoencephalitis* and was regarded as a complication caused by the attack of rubella.

Other severe complications associated with this disease have been noted by O. Potter (Brit M J 2 1084 (Dec 27) 1930). One woman of 40 years developed an acute *polyarthrititis* 3 days after the appearance of the rash and symptoms of rubella. The pain and swelling of the joints decreased 4 days later and by the end of 3 weeks had entirely disappeared. Another patient, a child of 5 years, had a generalized *convulsion with loss of consciousness* on the fourth day of an attack of rubella. The condition improved within a few hours and recovery was complete. The convulsion had been preceded by a very injudicious diet, which may have been responsible for this complication. In the third instance, a woman of 34, with a mitral stenosis, developed a typical attack of rubella and a concomitant *lobar pneumonia*. She recovered from both

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**SALICYLATES.—ADMINISTRATION.**—In commenting on administration of salicylates, G. H. W. Lucas and V. E. Henderson (Canad M A J 24. 541 (Apr) 1931) feel that an alkaline agent should be given at the same time, but they prefer *calcium carbonate* or *magnesia* with the salicylates in solution. This may be made more palatable by adding compound syrup of sarsaparilla or syrup of aqua mentha piperita.

**PHYSIOLOGICAL ACTION.**—K. E. Birkhaug (J Infect Dis 48 212 (Feb) 1931) found that a saturated solution of *sodium salicylate* has the power of neutralizing diphtheria and tetanus toxins *in vitro* without destroying their antitoxinogenic capacity. He found that the bactericidal action of the sodium salicylate on the more commonly encountered pathogenic microorganisms is about one-tenth of phenol. The exact mode of action of sodium salicylate *in*

effect is unknown. However, it has a dual capacity in that it acts as an antitoxic and an antiseptic agent. He believes that this may explain its therapeutic success in certain of the infectious diseases.

K. Gebert (Ztschr f klm Med 117:147 (June 22) 1931) studied the action of salicylates with the idea of ascertaining the cause of respiratory difficulties which are sometimes seen in salicylate therapy. He concluded that in moderate doses salicylates rarely cause respiratory symptoms and found upon examination of the blood that a reduction of the arterial carbon dioxide tension and an alkaline deviation of the blood reaction would occur even after doses of 6 Gm (1½ drams) of sodium salicylate. Gebert feels that simultaneous administration of sodium bicarbonate and salicylate is inadvisable because it likewise leads to blood alkalosis. Blood oxygenation is not influenced by salicylate medication.

O. E. Hagebush and R. A. Kinsella (Proc Soc Exper. Biol and Med 27:922 (June) 1930) found that *sodium salicylate* would suppress the allergic reaction to filtrates of a strain of *Streptococcus hemolyticus*. In studying cases of arthritis they found that those receiving salicylates did not show an allergic reaction to the intradermic injection of the isolated organism after a 10-day period, whereas such a reaction was observed in untreated cases.

**UNTOWARD EFFECTS.**—The cause of *acidosis* in salicylate treatment was studied by C. C. Johnson (J. A. M. A. 94:784 (Mar 15) 1930), who found that in the treatment of rheumatic fever, twice the dose of sodium bicarbonate with the salicylate is fully justified. In any *poisoning* from salicyl compounds the symptoms to be expected are those

of *acidosis* and treatment consists of **sodium bicarbonate** administered in any manner possible. He also feels that bicarbonate prevents local gastric irritation, as well as guards against *acidosis*.

In studying the signs and symptoms of overdose or intolerance to salicylate therapy, N. Morris and S. Graham (Arch Dis Child 6:273 (Oct) 1931) concluded that only where at least 60 grains (4 Gm) per day were given, were injurious effects noted. In these cases vomiting became a constant and early sign and often confused mental states and mental torpor were seen. Dyspnea was frequently seen but was not constantly present, it was acyanotic. Most cases showed acetoneuria. In those cases receiving concomitant sodium bicarbonate, the toxic symptoms were rarely observed and the authors believe it is unjustifiable to prescribe large doses of salicylate without giving in addition sodium bicarbonate.

A case of death following ingestion of 24 cc (6 drams) of *synthetic methyl salicylate* is reported by I. S. Meyerhoff (J. A. M. A. 94:1751 (May 31) 1930). Vomiting occurred early. Later, the child became dyspneic and cyanotic, the pupils were contracted and the pharynx and tonsils injected. Sudden pulmonary edema developed and despite intracardiac injection of caffeine sodium benzoate, the child expired. At autopsy, the chief pathological changes were cloudy swelling of the liver, hypertrophy of the intestinal lymph nodes and lymphoid tissue, a mild degree of acute nephritis, and congestion and edema of the lungs. He states that methyl salicylate should be dispensed only with the proper warning of the possible danger in its internal administration. His pathologic findings were very similar to those reported by other authors.

**SALPINGITIS.—GONORRHEAL.—Treatment.**—H. M. Little (Am J Obst and Gynec 20:582 (Oct) 1930) advocates the use of turpentine injections in the treatment of gonorrheal salpingitis. Permanent relief of pain was obtained in 90 per cent and in most of the cases the inflammatory masses disappeared in from 4 to 6 months.

The procedure employed by Little consists of opening the abdomen, protecting the peritoneum by rubber sheeting, and releasing the adhesions about the adnexa. Tubal masses are evacuated with a syringe with a large needle, after which the syringe is changed and the same needle used to inject a quantity of 10 per cent turpentine in oil. No attempt is made to prevent the solution from exuding into the pelvic cavity. The uterus is then suspended with silk, either by the Olshausen or Baldy-Webster method. In several patients a profuse uterine drainage was observed 3 to 4 days following the injection, indicating that an obstruction of the lumen of the tube at the uterine end had been overcome. It is not believed that the oil remains in the tube as a later operation in one patient failed to reveal any turpentine.

**TUBERCULOUS.**—From a study of tuberculosis of the female genital organs at Saranac Lake, E. M. Jameson (Am. Rev. Tuberc 22:72 (July) 1930) claims that this complication ranks fifth in frequency in women suffering from pulmonary tuberculosis. Signs or symptoms of pelvic inflammation in any women suffering with tuberculosis elsewhere should be viewed with suspicion.

Unless there has occurred a previous gonorrheal vulvovaginitis, salpingitis in the virgin should be regarded as tuberculous. About 8 per cent of women

with pulmonary tuberculosis have tuberculosis of the pelvic organs.

**Treatment.**—For therapy of pelvic tuberculosis in patients with obvious pulmonary disease, Jameson advocates the use of the x-ray as offering a conservative method of treating lesions of the uterus and adnexa. If the patient is too ill for this form of treatment, conservative treatment with hot douches, baking and general medical measures are effective in most cases, whereas surgical intervention is restricted to those patients not relieved by other methods. It should be borne in mind, however, that surgery may prove most efficacious in patients not having any lung involvement.

**SALPINGOGRAPHY.**—It is claimed by J. Novak (Zentralbl. f. Gynak. 55:1449 (Apr. 25) 1931) that salpingography is by no means the harmless and safe method of examination which many investigators claim for it and that in most cases it would be much simpler and less dangerous to employ the tubal insufflation test, in which only an absorbable gas is injected. Novak reports a case in which lipiodol was found in large amounts in closed tubes 15 months after it had been injected by way of the uterus for diagnostic purposes. The oil was found not only in the lumen of the tubes, but upon microscopic examinations was visible in the walls of the organs. There were no destructive changes however.

**SALPINGOSTOMY.**—W. T. Matwejew (Zentralbl. f. Gynak 55:302 (Jan. 31) 1931) claims that salpingostomy for the restoration of the tubal lumen gives encouraging results in selected cases in the absence of acute inflammation. In his technic the uterus



and adnexa are first liberated from adhesions. If there is a simple tubal closure the fimbria are separated widely by forceps, the tubal patency tested with a sound, and the separated fimbria sutured with 3 fine sutures in such a manner that the tubal mucosa is brought over the peritoneal aspect of the tube as much as possible and without injury to the delicate cells of the mucosa. In the presence of a hydrosalpinx a healthy portion of the tube is selected and clamped and the tube separated  $\frac{1}{2}$  cm medial to the clamp. The accompanying vessel is ligated and a new ostium is made on the healthy stump. A ventrosuspension of the uterus should always follow, since this serves to hold the tubes out of the pouch of Douglas so that they are not likely to become entangled in new adhesions. Following the operation, repeated tubal insufflations should be performed in order to maintain the patulous condition of the lumen.

**SACRO-ILIAC JOINT.** See JOINTS

**SCARLET FEVER.—ETIOLOGY.—Predisposing Causes.**—In tropical regions, Otto Fischer (Munch med Wchnschr 77 1749 (Oct 10) 1930) points out that scarlet fever is either entirely absent or extremely rare. The author performed the Dick test on 752 natives of Africa belonging to 5 different tribes. There were only 18 per cent positive reactions among the African natives examined, while among Europeans more than 60 per cent reacted to the test. F. K. Kleine and H. Kroó (Deutsche med. Wchnschr. 56:46 (Jan 10) 1930) observed that the blood serum of natives of East Africa contained scarlet fever antitoxin.

Five groups of the population characterized by a dominance of a particular race within the borough of Manhattan (children of native born white people, of native parents, of negroes, of Italians, of Russian-Polish, and of Irish parents) were studied by H. Emerson (J. A. M. A. 96 2153 (June 20) 1931) from the point of view of demographic characteristics, environmental factors, and the incidence as well as the death rate and case mortality, among children under 5 years of age, from scarlet fever and also from diphtheria and measles. So far as the statistical method can be used to offer evidence on this point, it seems that the factor of *race* is the only one of importance that can be recognized clearly as a variant of significance among the population groups studied.

H. von Willebrand (Am J Dis Child 41:1232 (May) 1931) observed that many cases of scarlet fever are present when the *atmospheric pressure* is low and that the disease is almost absent when it is high.

**Specific Cause.**—S. J. Zlatogoroff (Zentralbl. f. Bakteriol. 113.97 (July 8) 1929) concludes from experimental evidence that during the incipient stages of scarlet fever a *filtrable virus* is present in the faucial exudate which is capable of activating the otherwise avirulent hemolytic streptococcus to assume toxigenic properties. While Cantacuzéne (J. A. M. A. 95.673 (Aug 30) 1930) favors the theory that in general the streptococcus is the causative agent of the disease, he contends that the agglutination of nonscarlatinal streptococci by serum from scarlet fever convalescents can be explained only by the existence of a virus associated with and carried by the streptococcus. However, K. E. Birkhaug, L. V. Ackerman and W. M. Allen (Proc. Soc. Exper. Biol. and

Med 28:100 (Nov) 1930), as a result of experiments with laboratory animals, and T Toyoda, Y Futagi and M Okamoto (J. Infect Dis 48 350 (Apr) 1931), as a result of those with human beings, were unable to verify the observations of Zlatogoroff

Toyoda, Futagi and Okamoto (*loc cit*) produced *experimental scarlet fever* in human beings with positive Dick tests by inoculating their throats with apparently pure cultures of hemolytic streptococci obtained from scarlet fever patients. The rash produced by the infection gave a positive Schultz-Charlton reaction. The positive skin reaction to the heat-labile exotoxin gradually became negative during convalescence; at the same time, the negative reaction to the heat-stable endotoxin prior to the infection, became positive upon the patient's recovery. The blood serum obtained before inoculating the patients with the streptococci failed to produce a positive Schultz-Charlton reaction; however, serum obtained during convalescence produced a positive test

Although the hemolytic streptococcus has been more or less generally accepted as the specific cause of scarlet fever, there is considerable controversy as to whether or not there exists a particular strain, or a group of closely related strains of hemolytic streptococcus scarlatina which can be separated from other hemolytic streptococci. Some investigators, such as L. J. Hektoen (J. Bact. 19:57 (Feb) 1930) and D. Thomson and R. Thomson (Ann. Pickett-Thomson Research Lab. 6:1 (Dec.) 1930) contend that the specific cause of scarlet fever comprises a distinct and separate group of hemolytic streptococci. Ruth Tunncliffe (J. A. M. A. 94:1213 (Apr. 19) 1930; J. Infect. Dis. 48:511 (June) 1931) states that

hemolytic streptococci from typical cases of erysipelas and septic sore throat turn chocolate agar a bright green at temperatures below 34° C after 24 to 48 hours, while those from scarlet fever produce no change or occasionally a slight greening after several days' growth. V. D. Allison (Lancet 2 844, 1931) found that out of a total of 396 strains of hemolytic streptococci isolated from nonscarlatinal infections, only 8, or 2 per cent, were found by agglutination tests to belong to one or another of the 4 main serologic types of scarlatinal streptococci. The results, according to the author, indicate the high degree of specificity of the scarlatinal streptococci, as 63 per cent of hemolytic streptococci from scarlatinal patients can be typed serologically.

Mary W. Wheeler (J. Prev. Med. 4 1 (Jan) 1930) has found no really fundamental difference in the hemolytic streptococci isolated from various infectious processes. F. Green (Canad. M. A. J. 23 798 (Dec) 1930) was unable to distinguish scarlatinal streptococci from other hemolytic streptococci by means of the complement-fixation test. T. Toyoda, J. Moriwaki, Y. Futagi and S. Hoshizaki (Brit. J. Child. Dis. 27: 282 (Oct-Dec.) 1930) have concluded from morphologic, biologic and serologic studies that scarlet fever streptococci cannot be regarded as possessing a specificity that distinguishes them from other hemolytic streptococci. It may be, as a number of authors have contended, that specificity in the scarlatinal streptococcus may depend upon the capacity of the strain to produce an active toxin.

**Transmission.**—P. B. Brooks (New York State J. Med. 30:1418 (Dec. 1) 1930) has added another case of scarlet fever belonging in the milk-borne

group, apparently due to udder infection of the cow with the hemolytic streptococcus

**SCARLATINAL OR DICK TOXIN.**—R. Lopatizki (Jahrb. f. Kinderh. 126:241 (Jan.) 1930) states that the Dick toxin consists almost exclusively of exogenous bacterial toxin. From the washed streptococcus of scarlet fever, a very weak toxin may be prepared by maceration. Inoculation of washed streptococci into rabbits resulted in a serum that would not produce the extinction phenomenon. K. Ando (J. Immunol. 17:361 (Oct.) 1929), K. Ando, K. Kurauchi and H. Nishimura (*Ibid.* 18:223 (Mar.) 1930), K. Ando and K. Ozaki (*Ibid.* 18:267 (Apr.) 1930), and K. Ando and K. Kurauchi (*Ibid.* 19:99 (Aug.) 1930) have isolated 3 substances from the Dick toxin, namely a heat-stable, nontoxic bacterial protein; a heat-labile and a heat-stable scarlatinal toxin.

**Dick Test.**—According to P. S. Rhoads (J. A. M. A. 97:153 (July 18) 1931), the Dick test is a reliable indicator of immunity to scarlet fever. No case of the disease developed among 533 nurses found immune on original tests, while 15 cases occurred during the same period among 449 nurses who either were Dick positive or were not tested nor immunized. D. G. Lai (China Med. J. 45:749 (Aug.) 1931), in the spring of 1930, carried out extensive observations and performed the Dick test on 683 school children in Woosung, of which number 73 per cent. were found to have a positive test. One year later, using a supply of toxin obtained from the same source as the first, the Dick test was again performed on the school children. At that time only 26.8 per cent were positive. It is suggested that the difference may be

due to a diminished potency of the second supply of toxin.

According to Ellen F. Taylor (Canad. M. A. J. 23:56 (July) 1930), the Dick toxin loses its potency quickly and consequently the time limit marked on each package should be carefully observed. K. Ando (J. Immunol. 20:1 (Jan.) 1931) states that although the ordinary Dick toxin is usually very stable, it may deteriorate under some unknown condition. However, dried toxin, according to the author, retains its full capacity for a long period of time. As a standard toxin, the author recommends the adoption of a purified toxin, free from nucleoprotein and reduced to the dry state.

G. Herholz (Ztschr. f. Kinderh. 49:667, 1930) has little faith in the Dick test as a test for immunity or susceptibility.

According to Ando and his collaborators (*loc. cit.*) a reaction to the nucleoprotein in the Dick toxin indicates allergy, while a reaction to the scarlatinal toxin signifies susceptibility to scarlet fever. T. Toyoda, J. Moriwaki and Y. Futagi (Lancet 1:73 (Jan. 11) 1930) conclude that the Dick test is a reliable indicator of susceptibility to scarlet fever, the only exception being in those cases in which an allergic response develops to the heat-stable constituent of the Dick toxin.

#### **SURGICAL SCARLET FEVER.**

—In a few of the cases of surgical scarlet fever studied by T. Toyoda, J. Moriwaki, Y. Futagi and C. Kuroi (Am. J. Dis. Child. 41:1009 (May) 1931) no hemolytic streptococci were detected, the only microorganisms noted being hemolytic staphylococci. However, in such cases the rash produced was clinically not only distinguishable from the scarlatinal rash, but the

Schultz-Charlton test was negative. According to the authors, the rash caused by the staphylococcus toxin seems distinct from the scarlatinal exanthem.

**PATHOLOGY.—Blood.**—In the 7 cases of scarlet fever studied by A. Leonı (Riv di clin pediat 27:435 (June) 1929), the number of polymorphonuclear neutrophilic cells with 1 or 2 nuclear bodies was markedly increased during the eruptive stage. During the same period, the ratio of the polymorphonuclear neutrophils to lymphocytes was increased, but became normal during the stage of desquamation. In normal children the ratio was 1:1; in mild cases of scarlet fever it was usually 7:5:1, and in the severe cases, 20:1.

The *organic acid content* of the blood, according to E. A. Vladimirova (Ztschr. f. Kinderh. 50:374, 1930) is greatly increased early in scarlet fever, the increase depending somewhat upon the severity of the disease.

The *chlorine* content of the blood, A. A. Markowa (Ztschr. f. Kinderh. 50:496, 1930) states, is below normal in the early stage of scarlet fever. The degree of diminution is directly dependent upon the severity of the disease.

**Liver Function.**—S. van Creveld (Am. J. Dis. Child. 41:1231 (May) 1931) studied the function of the liver during the course of mild cases of scarlet fever. The study was carried out with respect to the carbohydrate metabolism, galactose and dextrose, as well as by watching the changes in the urine and in the blood. In the early stages few deviations were found in hepatic functions, and these were demonstrated only by means of galactose. Later on, during the fourth week, the frequency of the ability to demonstrate abnormality of the liver increased, but the relationship between the insuff-

iciency of fructose and of galactose remained the same. Investigations along the line of tolerance for dextrose did not give definite results. Tolerance of the liver for galactose was severely disturbed in the 14 cases of icterus occurring in scarlet fever. The author emphasizes that this is another reason for believing that patients with scarlet fever are not cured until at least the end of the fourth week.

**Spontaneous Extinction Reaction.**—Scarlet fever patients with old, healed pyogenic foci of the skin such as pustules, furuncles, impetigo, etc., often fail to develop a rash at the site of the lesion. G. Moriwaki (China Med. J. 42:286 (Apr.) 1928) refers to this as the spontaneous extinction phenomenon. H. Hentschel (Ztschr. f. Kinderh. 49:205, 1930) has applied the term of *active extinction* to the reaction.

**COMPLICATIONS.—Circulatory System.**—C. Shookhoff and L. M. Taran (Am. J. Dis. Child. 42:342 (Aug.) 1931) observed that the increase in pulse rate in scarlet fever was commensurate with the increase in temperature. A relative *bradycardia*, beginning in the second week and returning to normal at the end of the third week, was observed in 25 per cent. of the children. There was no prolongation of the P-R interval. Only minor changes in the T or the R-T wave were noted in 10 per cent. of the children. These changes returned to normal after the patient was discharged. An abnormal axial deviation occurring during the course of the illness was noticed in 16 per cent. of the children. The deviation of the axis returned to normal limits before discharge with one exception. These observations differ from those described in rheumatic fever in (a) the comparative infrequency of

electrocardiographic evidence of myocardial involvement; (b) the absence of any tendency for abnormalities, when present, to persist, and (c) the absence of prolongation of the P-R interval

*Endocarditis* was reported by G. L. Hallez (Bull. Soc. de pédiat. de Paris 27: 367, 1929) in 2 scarlet fever patients with arthritic manifestations. The author believes that rheumatic endocarditis is not of the same nature as that due to scarlet fever. Ina M. Richter (J. A. M. A. 97: 1060 (Oct. 10) 1931) has concluded from a clinical study that scarlet fever apparently is a factor in the causation of organic cardiac disease, the type of lesion found in these patients suggesting the myocardial lesion of later life.

*Symmetrical necrosis* was observed by G. Fedders (Jahrb. f. Kinderh. 129: 270 (Nov.) 1930) in a 4 year old child with scarlet fever. There was little general reaction and no other complication. The blood picture did not suggest sepsis. The skin was not sensitive to the Dick toxin. Two cases of *gangrene* complicating scarlet fever were reported by D. S. Sutherland (Brit. J. Child Dis. 27: 102 (Apr.-June) 1930).

**Nephritis.**—According to B. S. Hirschberg and M. E. Ssucharewa (Jahrb. f. Kinderh. 122: 340 (Jan.) 1929), nephritis may occur at any time during the course of scarlet fever. In fact, 11.9 per cent of all the cases of nephritis began during the first week of scarlet fever. The authors point out that it is difficult to harmonize the occurrence of early cases of the complication with the allergic theory of scarlatinal manifestations.

K. Birkhaug and R. Howard (Proc. Soc. Exper. Biol. and Med. 28: 95 (Nov.) 1930) found that the renal changes observed in rabbits following

intravenous injections of unconcentrated and concentrated scarlet fever toxic filtrates were not those of acute hemorrhagic glomerulonephritis. Instead, the changes were rather analogous to lesions observed in milder forms of tubular damage.

**Relapse and Second Attack.**—A. Lichtenstein (Notisk. Mag. f. laegevidensk. 91: 1133 (Oct.) 1930), since 1925, has observed an increase in the recurrence of scarlet fever, mainly in mild cases. Among 578 patients from 1925 to 1929 treated with scarlet fever antitoxin, a recurrent attack occurred in 36 or 6.2 per cent. A recurrent attack occurred in 136 or 9.3 per cent of 1462 nonserum treated patients, and in 3 or 1.5 per cent of 195 patients treated with convalescent serum. In a group of 450 serum-treated patients studied by J. D. Rolleston (Practitioner 125: 236 (July) 1930), only 1 developed a relapse. In more than 20,000 cases of scarlet fever observed by E. Gabriel and H. Zischinsky (Jahrb. f. Kinderh. 127: 253 (May) 1930) from 1902 to 1929, 387 cases (1.9 per cent) of second attacks occurred. As predisposing causes of second attacks, the authors observed wounds of various types (particularly burns), measles, chicken-pox, and serum disease. The course of the second attack, according to these authors, was usually more severe and complications more frequent than in the first attack. Specific treatment during the first attack does not prevent a second attack.

**DIAGNOSIS.**—The *Dick test*, according to Ellen F. Taylor (*loc. cit.*), may be employed as an aid in diagnosis. Until the rash starts to fade, the majority of scarlet fever patients will have a positive reaction; a week later, when immunity has developed, they will have

a negative reaction If the initial reaction is negative, one should be doubtful of the diagnosis However, Bernice Eddy and A G Mitchell (Am. J Dis Child 40 988 (Nov ) 1930) performed the Dick test on 546 patients with scarlet fever at various times during the acute febrile stage and during convalescence and found the results puzzling, in that the following 4 groups were encountered (1) that group in which a positive test became negative about the third to the seventh day of the disease and remained negative thereafter. (2) that in which a positive reaction remained so throughout the acute course of the disease and for as long as 5 weeks after the onset; (3) that in which the reaction was negative early in the disease and remained so throughout convalescence, and (4) that in which the reaction was positive at the beginning of the disease, became negative about the seventh to the tenth day, but again became positive during convalescence

**Schultz-Charlton Test.**—According to A. Stewart (Minnesota med 14: 537 (June) 1931), the Schultz-Charlton reaction is of definite diagnostic value, especially when the rash is well developed. Ellen Taylor (*loc cit.*) has found the test reliable in those persons not sensitive to the serum.

**Termination of Isolation.**—O Klingberg (Munchen. med. Wchnschr 76:1833 (Nov. 1) 1929) made repeated throat cultures for hemolytic streptococci from 184 convalescent patients before discharge A control group of 235 convalescents was discharged only on clinical observation. The percentage of return cases showed astonishingly little difference, being 3.4 and 3.2 per cent. respectively In addition, the author found that 3 patients who had no bacteriologic evidence of being scarla-

tinal carriers, upon discharge communicated scarlet fever to contacts at home

Ellen Taylor (*loc cit.*) states that the physician may feel safe in discharging scarlet fever patients with nonhemolytic streptococci in the nose and throat, but if cultures are positive for hemolytic streptococci, it cannot be ascertained whether it is a scarlatinal or a non-scarlatinal strain

From 50 to 60 per cent. of a group of scarlet fever patients studied by Mary Kirkbride, Mary Wheeler, and C. D West (J Infect Dis 47:16 (July) 1930) were found to be carriers of hemolytic streptococci at the end of the 30-day quarantine period Failure to find hemolytic streptococci, even when repeated examinations were made, could not be accepted as definite evidence of the absence of streptococci The clinical histories of 47 patients indicated that during the early stages of the disease between 20 and 30 per cent had probably been the source of infection to other persons However, only 2 (or less than 6 per cent.) of 34 patients who were carriers of hemolytic streptococci at the time they were released from quarantine apparently were the cause of return cases. According to these authors, a system of quarantine based on bacteriologic examination would be impracticable

**PROPHYLAXIS.—Active Immunization.**—G Herholz (Ztschr f. Kinderh 49 667, 1930) was unable to control scarlet fever in a closed institution by the use of the Dick toxin. The author could not state whether the toxin or its dosage, or the character of the epidemic were to blame

O. B Nesbitt (J A. M A 94 1490 (May 10) 1930) has been immunizing school children over a period of 5 years with the result that there has been a re-



duction of 29 per cent in the number of cases of scarlet fever and a 55 per cent reduction in the number of deaths P S Rhoads (*loc cit*) observed that in a group of 298 nurses who received the full 5 dose series of toxin injection, none developed scarlet fever, whereas, among 449 nurses who received no immunizing dose, 14 cases of the disease developed

M V Veldee (Pub Health Rep 45 1827 (Aug 8) 1930) states there are certain shortcomings in streptococcic biologic products that need correction before the health officer can afford to push their use energetically. According to the author, this in particular refers to the practice of giving 5 injections of toxins, low in potency and relatively high in protein content, which causes annoying reactions in a fairly large percentage of those treated. Until this defect is corrected, the use of these products by the physician remains limited and the public will not accept them to any great degree

H O McMahon (Am. J Dis Child. 39 66 (Jan) 1930) has used a scarlet fever toxoid in a course consisting of 3 injections. According to this author, the reactions to the toxoid are of no great consequence and at the same time the percentage of negative Dick tests compares favorably with other methods Y. Futagi (J Immunol 19:451 (Nov) 1930) has found reaction less frequent and less severe following the injection of anatoxin than after the injection of toxin M. V Veldee (Pub Health Rep. 46:693 (Mar 27) 1931), from experimental work, confirmed the findings of other workers in that the scarlet fever streptococcus toxin can be rendered much less toxic by subjecting it to heat and formalin. The antigenic value is apparently not destroyed by the de-

toxifying procedure. Furthermore, the amount of antigen tolerated by susceptible persons in each injection is greatly increased so that the number of doses required for active immunization may be reduced

Although G and Gladys Dick (Sajous's Analytic Cyclopedia of Practical Medicine, 10th Edit, Supplement, Vol 10, p 786, 1930) have warned against the use of Larson's ricinoleated antigen, W. R Shannon (Minnesota Med 14 47 (Jan) 1931) has injected it in combination with diphtheria toxin with very encouraging results. A complete course of treatment consisting of 3 doses had been given to 6953 children and an irregular course, 1 or 2 injections to 2205 more, making a total of 9150 children immunized. It was estimated that 4000 more children had been treated with the method by private physicians. It was estimated that in Minneapolis there were 105,000 children between the ages of 1 and 16 years. During the period of observation, 3973 cases of scarlet fever were reported. Of this number, 55 were in children who had received the vaccine. Scarlet fever was, therefore, 10 times as common among children who had not received the Larson's material. Somewhat similar results were obtained at the Gillett State Hospital for Crippled Children

**Passive Immunization.**—A Stewart (*loc cit*) has concluded from experimental work that there is no definite evidence to justify the use of scarlet fever antitoxin for the purpose of producing passive immunity. According to Schottmuller (Deutsche med. Wchnschr. 56:1159 (July 11) 1930), passive immunization with scarlet fever antitoxin gives immediate protection but is effective for only 2 weeks. George

F. Dick (Kentucky M. J 29 172 (Apr.) 1931) states that since persons who are immune to scarlet fever do not require protection, the indiscriminate administration of prophylactic doses of scarlet fever antitoxin is not justified. According to this author, if it is not possible to make skin tests and cultures of the nose and throat on blood agar to determine which contacts need antitoxin, it is better to watch all of them closely and to give a therapeutic dose of antitoxin on the development of any symptoms suggestive of scarlet fever. In the case of the susceptible contact who has received a prophylactic dose of antitoxin, active immunization should be begun 1 week after the administration of the serum.

**TREATMENT.—Serum.**—Ellen Taylor (*loc cit.*) states that if administered early, scarlet fever antitoxin shortens the initial stage. According to Margaret E. Wylie (J. Hyg. 30:331 (Aug.) 1930), the most striking result of the administration of the antitoxin was a rapid clinical improvement, as shown by the disappearance of the toxemic symptoms. T. Toyoda, J. Moriwaki, Y. Futagi and S. Hoshizaki (Brit J. Child Dis. 27:181 (July-Sept.) 1930) too, observed that the antiserum had a particularly remarkable effect upon the symptoms which are due to the streptococcus toxin, *viz*, rash, fever, itching, vomiting, convulsions and palpitation of the heart. The temperature and the pulse rate, according to these authors, fell sharply within a day after the injection. M. V. Veldee, F. E. Stevenson and A. G. Mitchell (Pub. Health Rep 46 3023 (Dec 18) 1931) observed that the period of eruption is shortened by serum therapy, and that desquamation tends to be localized and mild in the antitoxin-treated group, but

generalized and marked in the non-serum-treated patients. An analysis of the temperature readings failed to reveal any definite febrile reduction following the administration of antitoxin. Furthermore, E. G. Gabriel (Jahrb f Kinderh 131 148 (Apr.) 1931) observed that the much described "critical drop in temperature" occurred not only in those patients in whom serum was used, but also in the control series. However, even though the temperature does not fall by crisis to normal, J. D. Rolleston (*loc cit.*) points out that a remarkable improvement occurs in the general condition of the patient. The absence of considerable clinical improvement after serum therapy, A. Lichtenstein (Am. J. Dis. Child 40:549, 1931) states, is a fairly definite sign of the existence of a complication.

The frequency of complications, according to Ellen Taylor (*loc cit.*), E. Gabriel (*loc cit.*), A. Lichtenstein (*loc cit.*), and M. V. Veldee, F. E. Stevenson and A. G. Mitchell (*loc cit.*), is decreased by the early administration of scarlet fever antitoxin. Margaret Wylie (*loc cit.*), too, has found the serum to have some definite effect in reducing the incidence of nontoxic complications. According to W. R. Shannon (*loc cit.*), there is considerable doubt as to the value of the serum in preventing complications, the author stating that they are usually the result of bacterial invasion and are not of primary toxic origin. While J. D. Rolleston (*loc cit.*) contends that the serum has little if any value in preventing or curing complications, he was very favorably impressed by the action of serum in septic cases in which a tendency to ulceration of the fauces was apparently checked by this means. Margaret Wylie (*loc cit.*) could find no evidence that antitoxin

(a) diminished the occurrence of septic complications, (b) delayed the onset of either septic or nonseptic complications, or (c) shortened the duration of septic or nonseptic complications. However, Violet H. Comber (Lancet 1:698 (Mar 28) 1931) states that from the clinical viewpoint it appears to be clear that in any case in which there is reason to believe that septicemia may be streptococcal in origin, the repeated administration of scarlet fever antitoxin is well worth considering. On the other hand, A. Welch (New England J Med 204:968, 1931) contends that antiscarlatinal serum is of little more value than the same amount of distilled water after a case has once become septic.

In Stockholm, according to Lichtenstein (*loc cit*), the use of scarlet fever antiserum as well as convalescent serum has greatly modified the mortality rate of scarlet fever. Toyoda, Moriwaki, Futagi and Hoshizaki (*loc cit*) observed that the death rate was reduced by one-half with the use of antitoxin. Because of the rarity of severely toxic cases during the period of observation, Gabriel (*loc cit*) found it was impossible to form a definite opinion concerning the antitoxic action of the serum. Rolleston (*loc cit.*) states that the most striking example of the failure of the antitoxin was in Rumania, where the type of scarlet fever tends to be unusually severe and where much better results were obtained by the injections of convalescent serum than by the use of scarlet fever antitoxin.

The best therapeutic effects are obtained when the antitoxin is administered within the first 24 hours of the illness. According to T. Tsuda (Am J. Dis Child. 41:747 (Apr.) 1931), no effect is to be expected when the patient is given the injection 72 hours

after the onset of the illness. According to J. D. Rolleston (*loc cit*), in scarlet fever, as in all other diseases treated with antitoxin, it is important that the serum should be given as soon as possible, but it is a mistake to suppose that it is ineffective even several days after the onset of the illness. A. Lichtenstein comes to the same general conclusion, contending that the antiserum may be beneficial as late as from the fourth to the seventh day of the illness, and, in fact, as long as any toxic symptoms are present. T. Toyoda, J. Morowaki, Y. Futagi and S. Hoshizaki (*loc cit*) state that the best time for injecting serum is before the rash has turned dark red, regardless of the duration of the illness.

As W. R. Shannon (*loc cit*) has pointed out, there are 2 general opinions regarding the indication for serum therapy: (1) that the serum should be used in all cases as soon as the diagnosis can be made or even as soon as the disease is suspected, regardless of the severity, and (2) that the use of the serum should be limited to those cases that have marked toxemia at the beginning. According to George F. Dick (*loc cit*) antitoxin may be employed therapeutically with advantage in all cases of scarlet fever as soon as the appearance of the rash suggests the diagnosis. Given early in adequate dosage, it leads to brilliant results. Since the longer the patient goes without antitoxin, the less he benefits from the antitoxin when it is given, it should not be withheld until it becomes apparent that the attack is a severe one; it should be given in time to prevent the development of a severe attack. A. S. Stewart (*loc cit.*) on the other hand, has a rule that if the temperature is not over 102.5° F. (39.1° C) or if the patient

is not septic or toxic, he does not administer the antiserum

*Serum sickness* occurred in 44.8 per cent of the serum-treated patients of Ellen Taylor (*loc cit*), in 44.8 per cent of those of J. D. Rolleston, in 66.3 per cent of those of Veldee, Stevenson and Mitchell, and in 23 per cent. of those studied by A. S. Stewart (*loc cit*). The latter writer found that if he was obtaining more than the normal amount of serum sickness, investigation showed it to be due to some quality in the serum used, generally that it was not properly aged. This author has never been able to demonstrate any relationship between the degree of anaphylactic shock or serum sickness, and the previous administration of toxin-antitoxin. Veldee, Stevenson and Mitchell observed that a previous injection of serum seemed to be an important predisposing cause of serum sickness. Of those patients who had previously received serum in one form or another, 87.2 per cent developed serum sickness following the injection of scarlet fever antitoxin, while it appeared in 85.2 per cent of those patients whose previous injection of horse serum had been in the form of diphtheria toxin-antitoxin only.

### SCHIZOPHRENIA (DEMENTIA PRECOX).—TREATMENT.

—In a critical review of the psychoanalytic method of treatment, the broad statement of its limitations and usefulness are stressed by Alexander (*Arch Neurol. and Psychiat.* 26:815 (Oct) 1931). He states that periods of remission in the psychoses in general offer favorable opportunities for psychoanalysis. For the most part, psychoanalysts feel that a diagnosis of schizophrenia is a contraindication to this

method, but in recent years some attempts have been made in this direction, with results still to be weighed. Alexander feels that a variation of the technique employed for the neuroses may produce better results in dementia praecox. In the psychoses the patient "is so highly influenced by his subjective, nonadjusted demands, that he cannot accept a reality which is in contrast to his subjective demands and he falsifies the picture of the external world with which his senses and his normal thinking supply him." Carried to the extreme, the falsification is the hallucination or delusion, and the patient seeing in himself unacceptable (hostile or sexual) tendencies, denies them and projects them into others.

Alexander visualizes 2 conflicts in psychotic persons. The one is an infantile type: "The world is not what I should like to have it. I don't want to live in such a world and, therefore, I prefer to live in a fantastic one, I am ready to renounce real satisfactions and content myself with fantastic hallucinatory satisfactions, if only these are what I wish." The other conflict embodies tendencies which are not repressed but projected. "They are not recognized as belonging to one's own person, but as belonging to external reality." The delusions formed by this type of conflict are essentially paranoid and in such instances the patients show less deterioration of the ego than in the other type. The schizophrenic patient gets away from reality in his hallucinations and delusions, whereas the neurotic person cannot deny the reality and fights out the conflict within himself.

Because of the preservation of a part of the ego, the paranoid psychotic offers better possibilities in psychotherapy. The analyst produces a positive transference of the patient to himself as the

first step in bringing him into a better contact with reality. As time goes on, the transference is diffused to other objects of reality and the cure is thereby effected. The author prefers to call the method of treatment in these cases psychotherapy rather than psychoanalysis, thus indicating a departure from the routine employed in the psychoneurotic patients, but based on a psychoanalytic understanding.

Manfred Bleuler (*Arch Neurol and Psychiat* 26 610 (Sept) 1931) states the therapeutic ideas of his father (Eugen Bleuler) are somewhat as follows: "Psychoanalysis has no direct effect on schizophrenic patients. But he thinks highly of the indirect influence of psychoanalysis on schizophrenic therapy—on account of the contribution of psychoanalysis to the understanding of the disease in general and of the peculiarities of individual cases in particular."

Bleuler also refers to other forms of therapy employed in schizophrenia and in particular to the "sleep cure." He states: "Hypnotics are administered so that patients sleep almost constantly, awaking only for feeding and voiding. Usually the sleep should last from a week to 10 days. There is an element of danger in the sleeping cure, but this element becomes very slight under extremely attentive care of the physician and his nurse. The patient's physical functions, especially his diuresis, his respiratory organs and his pulse, must be constantly watched. It is of the greatest importance that no more of the hypnotic be administered than is absolutely essential for a quiet sleep. This means that the nurse must call a physician at any time, day or night, when the patient begins to awaken. It would be a grave mistake to give a pa-

tient, who is still asleep, a dosage sufficient to ensure sleep all night. By waiting until the sleep is finished, the physician may be able to use less hypnotics. Of course the cure must be interrupted immediately if diuresis becomes severe, if the patient ceases to expectorate, or if any other of his somatic functions becomes disordered. There is a choice of several hypnotics for these cures. We usually start the sleep with one dose of **scopolamine morphine** and a dose of 4 c c (1 dram) of a derivative of **allyl-isopropyl barbituric acid**, administered intramuscularly, or a dose of 0.4 Gm (6 grains) of **sodium phenobarbital** may follow. The additional doses have to be determined by the patient's weight, sex, general physical condition and, particularly the depth of his sleep and his individual sensitiveness to the hypnotic.

"The effect of the sleeping cure is purely psychologic, just as are all other therapeutic measures in schizophrenia. Its purpose is to prevent the schizophrenic peculiarities from becoming fixed and to give the patient the chance and the motive for a new and better adaptation. Therefore, the psychologic treatment, which must begin at the moment of awakening, is of greatest importance. Now the physician strives to interest the patient in his surroundings and to get in touch with him. The sleeping cures are indicated, naturally, in only a small number of cases, namely, when the patient does not improve in his behavior after an acute episode, in spite of the absence both of acute signs and of signs of deterioration."

**SCLERITIS.—ETIOLOGY.**—T B Holloway and W. E. Fry (*College of Physicians of Philadelphia*, Jan 15, 1931; *Am J Ophth.* 14. 1055 (Oct.)

1931) report a case of unsuspected brawny scleritis in a luetic patient, aged 49, who had a retinal detachment with secondary glaucoma. He gave a history of pain and redness of the eye but no history of trauma. Vision was reduced to light perception. Microscopical study of sections showed brawny scleritis.

**SCLERODERMA.—TREATMENT.**—J. Sellei (Med Klin 26 1859 (Dec 12) 1930) reports 8 cases of scleroderma uncomplicated by Raynaud's disease which were treated by pancreatic extract with favorable results. He suggests giving tablets of the dried pancreatic gland in doses of 0.25 Gm (4 grains) daily; later this is followed with the raw pancreatic gland, the gland being cut in small pieces and given in bouillon 35° C. (95° F.). (If given in hot soup, the ferment is destroyed.)

Scleroderma associated with Raynaud's disease and the scleroderma associated with leg ulcers and phlebitis are not benefited by the use of pancreatic gland. Good results were obtained by the writer in Raynaud's disease by the use of insulin injections plus pancreatic hormones plus dried pancreatic substance. Four to 6 weeks of treatment are necessary before any improvement is noted and it should be continued over a period of months.

**SEASICKNESS.—ETIOLOGY.**—In an extensive study of the mechanism of seasickness as related to the internal ear, Arne A. Sjöberg (Acta. Oto-Laryngol. Supp 14, pp 1-136, 1931) finds that there is every probability that the symptoms of seasickness are not induced by angle-acceleration, or what he has referred to as the *compound screwing motion* in the general ship's move-

ment, but that the symptom-complex is produced by the space movement (composed of plunging and harmonic swinging movement—both in the vertical and horizontal planes—in rolling or pitching), and in small vessels possibly combined with the progressive, irregularly accelerated horizontal movement. On a normal-sized passenger vessel in a high sea, the maximum acceleration values for the accelerated ship's movements in a horizontal direction are considerably higher than the corresponding values for the movements of a railway-train, but the maximum acceleration values for the movements in a vertical direction are in about the same order of magnitude as the corresponding values for elevators in general.

The symptoms of experimental seasickness ("elevator sickness") in human beings correspond exactly with those of seasickness. Deaf-mutes with reactionless labyrinths are not affected by elevator movements. Experimental seasickness with dogs can be easily provoked when the animals are exposed to rapid movements up and down in a crane. The clinical aspect of experimental seasickness with dogs is characterized by: greatly increased salivation, polypnea, diarrhea, polyuria, great agitation in the beginning and, when the symptoms are fully developed, apathy leading to asthenia, and usually vomiting. All the animals upon which investigations were carried out showed symptoms of experimental seasickness. With repeated experiments the animals became somewhat inured to the elevator movements. Puppies are immune to elevator movements. Labyrinths which are capable of functioning must exist for symptoms of seasickness to appear.

Optical and kinesthetic impulses will not be necessary for the symptoms of



seasickness to appear, but these impulses together facilitate and promote the appearance of the symptoms from the vestibular apparatus which is capable of functioning. Possibly optical impressions facilitate the symptoms to a greater extent than do the kinesthetic impressions. When a person is exposed to rectilinear horizontal and vertical movements with varying accelerations, or to the movements of a ship in a high sea, pressure variations, with the accompanying displacements and currents in both the perilymph and the endolymph, must make their appearance at every point of the contents of the labyrinth, both in the fluids and, particularly, in the walls of the labyrinth.

These pressure variations affect both labyrinths at the same time, but the momentary pressure in the corresponding points of the 2 labyrinths will seldom be exactly the same during the motions of a ship in a high sea. It seems very probable that the pressure variations in labyrinths in rectilinearly accelerated vertical movements, and the combined pressure variations in the movements of a ship in a high sea with the intralabyrinthine physical phenomena caused by them, are probably of such an order of magnitude that it may be possible that they irritate the sensory epithelium so intensively that fully typical symptoms of seasickness supervene.

It thus seemed justifiable to Sjöberg to presume that the complex of seasickness symptoms arises from the whole vestibular apparatus, both from the semicircular canal system and the otolithic apparatus. The adequate irritation methods for the sensory epithelium is thus thought to be, firstly, the pressure variations with their currents and displacements within the fluids of the labyrinth, and secondly, the pressure

variations and displacements in the nerve-end areas themselves within the vestibular apparatus. It is extremely probable that small reflex eye movements, invisible to the naked eye, occur in the case of rectilinearly accelerated vertical movements. There is a great probability that during the movements of a ship in a high sea similar small eye movements occur, although they cannot be observed by ordinary macroscopic observation. Headache and some of the psychic symptoms accompanying seasickness may be largely due to the intracranial pressure variations caused by the movements of a ship, which affect the brain and its various centers.

#### SERUM THERAPY AND SERUM SICKNESS.

— In discussing the value of various convalescent serums, E. G. Morales and O. Costa (Am J Dis Child 39:1-214, 1930) state that they have had very good results in the prophylactic use of *convalescent measles serum* but that use of a new adult serum showed very little evidence that it is of material benefit. In a large percentage of children treated with *immune adult serum*, however, about 80 per cent. showed immunization from the disease through familial exposure, whereas among a group of controlled children only 18 per cent. failed to contract the disease on familial exposure.

As to the value of immune serum in pathological conditions due to the *Bacillus coli*, it is the opinion of H. Vincent (Riforma med. 46:1423 (Sept. 8) 1930), that a specific serum can be developed and that this antibacillary serum therapy effects a cure in many instances. This serum must be developed by both the endo- and exotoxins which are found in colon bacilli.

An attempt has been made by A B Sabin and G B Wallace (J Exper Med 53 339 (Mar) 1931) to prove that chills seen during serum therapy are not anaphylactic in type, but that some principle is present which cannot be filtered out, taken out by dialysis or by heating, but which only occurs when the blood and serum have been allowed to set for some time before being re-injected

From a study of the effect of injections of *antipneumococcic serum* in monkeys and dogs, J A Kolmer and K W Amano (Arch Otolaryng 14 125 (Aug) 1931) find that in virulent Type I pneumococcic meningitis, prophylactic serum has some value. In the Type II and Type III pneumococci the specific antipneumococcic serums are less valuable in preventing meningitis. They feel that all cases of chronic infection of the sinuses and mastoids which are to be operated upon should have the causative organisms isolated and prophylactic serum therapy either started or ready to start before operation is done. They believe that such a procedure would lessen quite materially the occurrence of meningitis and, if it should occur, it would lessen the severity of the disease.

The present status of *convalescent serum therapy* is discussed by W H Kellogg (J A M A 93:1927 (Dec 21) 1929), who feels that a passive immunity can be produced in both **measles** and **anterior poliomyelitis**. This immunity, if only partial, will at least mitigate the severity of the attack. He believes that in poliomyelitis the serum should be given intraspinally and that the danger of spinal puncture can be disregarded.

**SERUM SICKNESS.**—In commenting on the occurrence of serum sickness, W Balaban (Arch f Kinderh 91:193 (Sept 19) 1930) feels that the

intensity of a first attack is determined by the constitutional characteristics of the organism. Occasionally this takes the form of an anaphylactic shock and may occur immediately after injection, but more often it is seen from 1 to 2 weeks after the injection. When the nervous system is affected, pronounced changes occur in the vasomotor system and in the sensory peripheral nerve endings.

In the opinion of G M Mackenzie and F M Hanger (J A M A 94 260 (Jan 25) 1930), about 10 per cent of persons have no notable manifestations of serum sickness even after injection of large doses of serum. They find that the North American Indian and the negro have a very low susceptibility to serum sickness. In many cases where it is most pronounced the incubation period is usually from 6 to 12 days, a previous injection of the serum, however, may shorten this incubation period. The usual symptoms are urticaria, rash, rise of temperature for 48 hours, albuminuria, cylindruria, and leukocytosis. Optic neuritis and polyneuritis may occur. In some instances, a relapse has been observed. Serum accidents, on the other hand, may be mild or severe. They may occur while the serum is being injected before the needle has been removed, or they may appear from 1 to 2 hours later. They are most often seen in those individuals who have had previous serum therapy or from the type known as horse-asthmatics, *i.e.*, those susceptible to horse dander, etc.

Mackenzie and Hanger feel that in all cases of serum treatment, a careful history should be obtained regarding the previous employment of serum therapy and regarding any sensitivity of the patient to various types of anaphylaxis. They also feel that a preliminary skin

test should be made before injecting large amounts of serum and if the test is positive, the patient should be very carefully desensitized before proceeding with the therapy. In all cases a supply of epinephrine should be kept available for immediate use in case of *anaphylactic shock* and there should be no hesitancy in repeating the dose of epinephrine if necessary.

**SHINGLES.** See HERPES ZOSTER

**SKIN.—SELF-STERILIZING POWERS.**—It is obvious that the skin has remarkable powers for freeing itself of the constant and ubiquitous organic contaminations by which it is beset. In tests of this power made by Theodoie Cornbleet and B. E. Montgomery (Arch. Dermat. and Syph. 23:908 (May) 1931) it was found that normally dry skin, open to the air and intact, showed little variation as regards location of area tested, except that the vicinity of the nails showed it less. More than 73 per cent of the sterilization is accomplished in the first 10 minutes. When denuded of epithelium this power is lessened. It would, therefore, seem to reside in the epithelium, but where this is the thickest, *i.e.*, palms and keratotic areas, there is no increase of sterilization. Perhaps this is because only the superficial layer, in actual contact with the bacilli, has this function. Moist folds show a decreased capacity. There is evidence to show that poorer results were effected as the lower layers of the epithelium were exposed. Intact skin over keloids, hemangiomas, and young deep granulomas responded normally. Ultraviolet rays applied to the normal skin impart no added sterilization power to it.

The skin of patients affected with yeast infections and erosions, *perleche*,

or *erosio digitalis saccharomycetica*, showed decreased power both over the lesions and on unaffected areas of skin. This may account for spread of infection. Such persons appear to undergo cyclic variations in their capacities for sterilization of the affected areas against yeast.

Psoriatics show less resistance over affected areas than on their normal skin areas, which latter gave the same response as those of normal persons. Experiments showed that organisms on unaltered psoriatic lesions had a better chance to survive than did those on lesions freed from scales.

Intravenous injections of 10 c.c. (2½ drams) of 1 per cent gentian violet aqueous solution varied the sterilizing power of psoriatic lesions to an equality with that of unaffected skin in the same individual.

In furunculosis, the organism (*Staphylococcus aureus*) seemed to enjoy a certain degree of immunity to sterilization by the skin of affected persons, although yeast fungi are destroyed as by normal skins.

Doses of 1 c.c. (16 minims) of 1 per cent. manganese citrate, intramuscularly, when given at weekly intervals caused a final higher level of resistance in the skin to *Staphylococcus aureus* than had existed before the injections. There was a depression of the skin's power of sterilization immediately after the injection, but at the end of a week it had risen above the original capacity.

**SMALLPOX.—MORBIDITY.**—The incidence of the severe types of smallpox in the United States and in Europe has declined during the past few years but the milder forms of the disease, termed *alastrim* or *amaas* by some writers, are still quite prevalent. Cer-

tain clinicians have claimed that there are essential differences between the latter mild types and true smallpox, and that they should be considered as 2 different diseases. However, the lesions produced by both of them are identical histologically, and according to J McIntosh (Lancet 1 618 (Mar 22) 1930), the serologic findings are the same, the only differences being those of cross immunity. He has observed that a successful vaccination will protect thoroughly against the mild types of smallpox such as have been called *alastrim*, but that an attack of the latter disease does not always give assurance that a subsequent vaccination will not take.

**COMPLICATIONS.**—Because of the recent increase in the number of encephalitic complications following *vaccination* in parts of Europe, it is interesting to note a report of a similar complication of smallpox itself. A G Troup and E W Hurst (Lancet 1:566 (Mar. 15) 1930) report the instance of a man of 63 years of age who developed a mild attack of smallpox which was followed on the twelfth day of his illness by a retention of urine, a flaccid paralysis of the lower extremities, drowsiness, headache and fever. Death occurred about 4 weeks later and necropsy showed a perivascular infiltration of the brain and a myelin degeneration similar to the changes present in postmeasles and postvaccinal encephalitis. The investigators reviewed the case histories of 140 patients who died from smallpox between the years 1925 and 1929 and discovered that many of these patients had had symptoms referable to the central nervous system, such as convulsions, hemiplegia and coma. Clinicians have referred previously to certain nervous symptoms which they have observed in connection with smallpox, such as

ataxias, mental changes, paraplegias, and disturbances of sensation, so that it is possible that encephalitic complications are more common than formerly supposed.

One of the less common complications of smallpox has been reported from 2 sources during the past year. P Lombard (Rev d'orthop 16 490 (Nov) 1929) described a case of *osteoarthritis* in a boy, 7 years of age, who had developed abscesses in the elbow joint which resulted in an ankylosis; and another case, in a boy of 13 years, with multiple *bone lesions*. Both patients had had an attack of smallpox which seemed to coincide with the probable time of the onset of the bone infection. C F Eikenbary and J F LeCocq (J. A. M. A 96 584 (Feb 21) 1931) observed 3 children with *bone lesions* which had probably started with an attack of smallpox several years previously. The characteristics of these lesions were premature closures of the epiphyseal ends of long bones, especially the femur, radius and ulna. In 1 instance the x-ray showed evidence of an old destructive process. The authors were inclined to believe that the lesions in these 3 instances were caused by aseptic abscesses of smallpox.

## **SMALLPOX, VACCINATION.** **—ACTION OF VACCINE VIRUS.**

—The nature of vaccine virus and the mechanism of the production of immunity has been the subject of numerous recent investigations. G. M Findlay (Brit J. Exper. Path. 12.9 (Feb) 1931) performed a series of experiments which indicated that the antivaccinia properties of blood serum resided in the globulin fraction of the blood. Rabbits, made *immune* to vaccinia by vaccination, were bled and their

blood serum divided by ammonium sulphate precipitation into its globulin and albumin portions. Each portion was mixed with vaccine virus and susceptible animals were inoculated. The virus was inactivated by the globulin fractions in low dilutions. Flocculation and phagocytosis experiments also indicated that the globulin portions contained the antibody, while the albumin portions did not.

L. C. Havens and C. R. Mayfield (Am J Pub Health 21:329 (Apr) 1931) report the presence of definite precipitins in the blood of rabbits vaccinated against smallpox by intradermal and intravenous methods. Four persons acquired sufficient amount of these precipitins in their blood serum to flocculate vaccine virus 10 days after vaccination.

**METHODS.**—During the past year *intracutaneous* vaccination has been employed frequently and there has been considerable variation of opinion regarding its merits. In a small group of 4 infants, B. Bendix (Ztschr f. Kinderh 48:694, 1930) used intradermal injections of a vaccine lymph diluted 1:500 and in 1 instance noticed marked local and generalized reactions. The author concluded that he could not recommend the method for general use. In a larger series of observations, however, F. Gierthmühlen (München med. Wchnschr 77:1703 (Oct 3) 1930) obtained very satisfactory results. In some 300 trials he found that infection was no greater than with the cutaneous scratch method, but he emphasized the fact that each sample of material should be standardized before its general use. He employed dilutions of 1:50 which he recommended for the usual vaccination. Often higher dilutions gave more severe reactions than this concentrated form.

An interesting series of experiments

which tend to demonstrate that the scratch method of vaccination gives the greater immunity was performed by O. Kirsch (Ztschr f. Kinderh 49:1, 1930). He observed that in the revaccination of a group of children after a period of 5 to 7 years, those who had intracutaneous vaccinations previously had a much higher percentage of "takes" than those who had been vaccinated by the usual scratch method. The author believes that the effectiveness of the "take" depends on the development of a pustule on the skin. He concludes that the intracutaneous injection of vaccine lymph is less frequently attended by sepsis, but that the incidence of encephalitis as a complication is not reduced.

**COMPLICATIONS.**—Several rare forms of complications following vaccination have been reported during the last year. M. Vieu (Ann de dermat et syph 1:873 (Aug) 1930) observed vaccine lesions in the form of *ulcerations on the tongue* and, according to his review of the literature, this is the fourteenth such case reported. *Infection of the eyes* from the careless use of vaccine lymph were observed by P. Toulant (Paris méd 2:190 (Sept 6) 1930). If the material was accidentally inoculated on the lid, on the conjunctiva or on the cornea, the respective blepharitis, conjunctivitis, or keratitis might result. He reviews some 27 cases of such infections which have been reported in the literature up to this time.

The effect of vaccination on patients suffering from another disease has always been a debatable question. Further statistics in regard to this subject have been reported by R. E. Stone (Am. Rev. Tuberc 23:706 (June) 1931). Because of the occurrence of smallpox within the vicinity, he was forced to

vaccinate 337 institutionalized patients suffering from tuberculosis. All of the various stages of the disease were represented by the group. Three patients of the entire group reacted unfavorably, 2 having temporary exacerbation of the symptoms of cough and expectoration, and 1 developing a definite extension of the pulmonary lesion. The author concluded that if there is a definite exposure of such patients to smallpox, the procedure of vaccination is justified. However, W. Blacher (Jahrb. f. Kinderh. 130:201 (Jan.) 1931) observed 2 instances in which vaccination apparently activated a latent disease, 1 patient subsequently succumbing to a fatal meningitis and the other suffering from an exacerbation of a latent tuberculous focus in the lungs.

T. W. Brockbank (J. A. M. A. 97:227 (July 25) 1931) reported the case of a patient who developed symptoms of *myelitis* 11 days after vaccination. There was a loss of sensation below the level of the umbilicus and flaccid paralysis of the legs, which did not improve in the succeeding 6 months that the patient was observed.

H. D. Chalke (Lancet 1:578 (Mar. 14) 1931) observed 14 patients, aged 2 to 14 years, recently vaccinated who had 'skin rashes' of some sort. Six had maculopapular rashes somewhat morbilliform; a few had an urticarial type of eruption; 3 had papules and macules rather like rubella, and 1 had 20 to 30 papules surmounted by a crust which were distributed over the legs and arms with a few on the face and trunk. In one, the rash was limited to the vaccinated arm. These eruptions usually appeared on or about the eleventh day and had to be differentiated from modified smallpox, measles, rubella and scarlet lichen urticaria. The author be-

lieved most of the rashes were due to: (1) absorption of secondary products from the vaccine pustule, or (2) protein rashes. Generalized vaccinia is rare and is probably due to autoinoculation.

**Postvaccinal Encephalitis.**—*Incidence.*—There does not appear to be any decrease in the number of postvaccinal encephalitis complications, especially in Holland and England. E. Bienenstein (Ztschr. f. Kinderh. 49:248, 1930) estimates the incidence of encephalitis to the number of vaccinations as 1:100,000 in Germany, 1:48,000 in England, and 1:4000 in Holland. Reports from Holland (Am. J. Dis. Child. 39:1304 (June) 1930), reviewing the 47 instances of postvaccinal encephalitis which occurred between the months of July and October of 1929, which represented 1 such complication in 1684 vaccinations, show that no such complication was observed in the children under 1 year of age and that the incidence became greater as the age increased. The statistics indicated that the chances of a child contracting postvaccinal encephalitis were 4 times greater at the ages of 6 to 11 than at the age of 2 years.

A question has been raised by F. T. Grey and W. M. Whittaker (Brit. M. J. 1:1125 (June 21) 1930) whether all the instances reported as postvaccinal encephalitis had been definitely proved as such. They cite a case in which such a diagnosis was made and which was proved at necropsy and with blood cultures to be a septicemia following vaccination. A strain of staphylococcus was isolated and small abscesses were found in the brain substance. In another instance a man developed a pyogenic osteomyelitis and a septicemia immediately after vaccination. The true



underlying disease in this patient was possibly a lymphatic leukemia. The authors recommend that all patients with the symptoms of encephalitis after vaccination be hospitalized at once for a complete study to investigate these other possibilities of infection.

*Etiology*—Joseph Ungar (Casop lék česk 67 1669 (Nov 30), 1791 (Dec 28) 1928, Am. J Dis Child 42:905 (Oct) 1931) summarized the prevailing explanations for the occurrence of encephalitis following vaccination as follows: (1) A noxious material in the lymph; (2) activation of a latent focus; (3) a specific toxin; (4) a coincidental infection, (5) a combination of 2 infections, and (6) infection by contact.

In animals, at least, the vaccine virus itself apparently produces the disease, according to the experiments of A. Eckstein (Ztschr f Hyg u Infektion-skr 112:151, 1931). He injected vaccine lymph suboccipitally into monkeys and produced lesions which histologically appeared to be a meningoencephalitis.

Further studies of the etiology of postvaccinal encephalitis have been made by E. Gildemeister and P. Hilgers (Deutsche med Wchnschr. 56:312 (Feb. 21) 1930), who demonstrated the presence of vaccine virus in the spinal fluid of rabbits 6 to 12 days after they were vaccinated. The virus was observed in only 5 out of a group of 34 animals. P. A. Clearkin (Brit J Exper Path 11:329 (Oct) 1930) injected the vaccine lymph intradermally into a certain species of monkeys which had not been in contact with man before and, after the use of moderately large doses, was able to produce changes which were very similar to those occurring in human postvaccinal encephalitis. There was perivascular infiltra-

tion with an accumulation of the glial cells and a meningeal thickening, but the characteristic degeneration of the myelin sheaths was absent.

The production of postvaccinal encephalitis in monkeys has been attempted by reducing the vitality of the animals by hunger, chronic alcoholism or by removal of the spleen. A. Eckstein and M. Sarvan (Ztschr f Hyg. u. Infektion-skr. 111:659 (Nov 18) 1930) found that the animals which had been fasting reacted more slowly to the ordinary vaccination than control monkeys, but in none of the animals did any evidence of encephalitis occur. J. McIntosh and R. W. Scarff (J Path and Bact 33 483 (Apr) 1930) have produced typical encephalitic lesions in rabbits by intradermal, intravenous or intrathecal injections of the virus.

*Treatment*—In regard to the treatment of postvaccinal encephalitis with human convalescent serum from persons who have had a recent vaccination "take," there are an increasing number of favorable reports. J. Hekman (Nederl. tijdschr v geneesk 2:4774 (Oct 12) 1929; Am J Dis Child. 39: 649 (Mar) 1930) reports 10 cases of encephalitis following primary vaccination and 2 after revaccination. The last 2 were atypical both in their short incubation periods and in the atypical microscopic changes of the brain tissue. All of these patients were treated with 10 c.c. doses of serum from recently successfully vaccinated persons, the parents, if possible. The serum was given intravenously and the author believes there was a great improvement in the clinical course. Gruneberg (Klin. Wchnschr. 9:1127 (June 14) 1930) gave serum in similar doses, repeating the injection in 3 or 4 days, to 2 children who had severe attacks of enceph-

alitis following vaccination Both patients recovered

#### PREVENTION OF COMPLICATIONS OF VACCINATION.—

Blood serum containing antivaccinia bodies has been mixed with active vaccine virus and the mixture used for vaccination The principle of the method is similar to that of diphtheria toxin-antitoxin mixtures in that the active toxic material of such a solution is liberated slowly in the body and very little reaction, but complete immunity, results C P. Rhoads (J. Exper. Med 53:185 (Feb.) 1931) employed such a method on rabbits He neutralized vaccine with immune serum so that intradermal injection produced no reaction and gave the animals 2 subcutaneous inoculations of 2 c.c. each at intervals of 4 days, and instilled the material intranasally 3 to 5 times at intervals of 1 to 2 days With the latter method, no local lesions were produced on the nasal mucous membrane and only occasionally did a slight general reaction occur. No reaction occurred with the subcutaneous route With both methods, immunity was produced

M. Weinberg (Compt rend. Soc de biol. 106:624, 1931) also reported the results of vaccination by vaccine virus mixed with an equal quantity of serum from a rabbit made immune by repeated vaccination intradermally, intraperitoneally and intravenously. Patients vaccinated with this mixture by a single cutaneous scratch 5 mm in length had a cutaneous reaction consisting of very small vesicles, very little general reaction, little or no fever and the resulting scar was only a punctate cicatrix. Intradermal vaccination resulted in a small area of redness with only slight fever, and in other instances a small nodule which disappeared in about a

month These children were immune to subsequent scarification vaccinations

Similar experiments were performed by G M Findlay and E Hindle (Brit M J 1 740 (May 2) 1931), who combined immune rabbit serum and active vaccine virus and gave 4 intradermal injections to 2 rabbits The animals had either a slight hyperemia or a few punctate vesicles, but no significant general reactions or rise in fever Subsequent inoculations proved that these animals had been made immune The immune serum dilution is an important factor: 1 to 40 usually being too high, while 1 to 20 is ordinarily low enough to retain sufficient immune reaction of the serum

**SODIUM AMYTAL.** See ANESTHESIA, BASAL

**SODIUM DEHYDROCHOLATE.—CHOLAGOGUE ACTION.**—R F Sterner, H J Bartle and B B V. Lyon (Am J M Sc 182 822 (Dec) 1931) have reviewed the literature on bile salt metabolism and their experience with sodium dehydrocholate as a cholagogue Cholagogue action refers to the volume of bile output without regard for the quantitative amounts of the various constituents, *i e*, bile salts, bile pigments, cholesterol, certain inorganic salts, and water Choleretic action, on the other hand, has to do with the various amounts of biliary constituents other than water. Previous work has shown that bile salts in themselves are the chief and practically the sole bile secretory stimulants The metabolism of these bile salts is theoretically influenced by 3 major factors, according to these writers: (1) exogenous, embracing principally foods and drugs; (2) endogenous, including especially the effects of endocrine secretion

and nitrogen or protein metabolism, (3) the enterohepatic factor

*Exogenous factors* influencing bile salt metabolism are largely dietary. In the dog it has been shown that food protein is of foremost importance in determining the level of bile salt output. Other foods having cholagogue action are raw egg white, boiled egg white, fat, oil, soap solution, acids, Witte's peptone, and meat extractives, according to work cited by these authors. Tryptophane, isatin, and indigo, when added to the diet of dogs, cause a marked cholagogue effect. Bile salts themselves, as previously mentioned, are strong stimulants of bile flow when given by mouth or parenterally. Certain drugs, long supposed to have cholagogue powers, have proved inefficient by test. These include calomel, hydrochloric acid, sodium salicylate, and ethyl alcohol. F. S. Smyth and G. H. Whipple (J. Biol. Chem. 59:655 (Apr.) 1924).

The *endogenous factors* influencing bile salt metabolism seem to be closely associated with body protein metabolism. The authors point out evidence suggesting that body and food proteins are the sources of an essential precursor substance in bile salt synthesis.

The *enterohepatic factors* are concerned with the circulation of bile salts, including their secretion by the liver cells, their discharge into the duodenum, their reabsorption by the intestinal mucosa, and their subsequent resecretion by the liver cells.

Bile salt synthesis in the body seems mainly dependent upon the presence of cholic acid, according to the writers. The indol ring of indigo and isatin may be the source of cholic acid. Taurin, probably derived from cystin, apparently has a strong affinity for cholic acid and taurocholic acid results. Glycocoll

also may be formed within the body, and uniting with cholic acid forms glycocholic acid.

Bile salts generally are very toxic, being dependent, these authors believe, upon the cholic acid radical. Neubauer and Pohl found that apocholeic acid, desoxycholeic acid, dehydrodesoxycholeic acid, and dehydrocholeic acid were the only bile acids which were effective stimulants to bile secretion and yet were relatively nontoxic. The most efficient was dehydrocholeic acid. E. G. Wakefield, H. P. Powelson, C. S. McVicar (Ann. Int. Med. 3:572 (Dec.) 1929).

The effect of intravenous injection of 10 c.c. (2½ drams) of a 20 per cent. solution of sodium dehydrocholate (*decholin-sodium*) and estimation of bile flow by means of duodenal drainage was studied in 21 patients. All patients were again studied after a week to obtain control figures. It was found that the average flow of bile over a 90-minute period after decholin was 134 c.c. for each patient. The average flow for the same period without decholin was 80 c.c. Untoward effects were noted in 2 instances, 1 patient with myocardial damage, arteriosclerosis, and hepatic cirrhosis, developed edema of the face, tremor, and mental symptoms while another patient with cholecystitis developed abdominal pain within 48 hours.

The writers conclude that sodium dehydrocholate (*decholin-sodium*) in 2 Gm. (30 grain) doses intravenously increases the flow of bile obtained by duodenal drainage which is probably dependent upon an increased flow of liver bile.

#### SPINA BIFIDA OCCULTA.—

Spina bifida occulta occurs in the adult in from 1 to 3 per cent. of cases. In

infants it may be as high as 91 per cent. In considering the biological aspects there is noted a tendency toward familial occurrence.

An important factor is that this region is undergoing a marked phylogenetic change, according to R. J. Dittrich (*Surg Gynec. Obst* 53:378 (Sept) 1931), and organs undergoing physiological changes are of course more prone to exhibit variations. Willis, in a study of 1471 skeletons, found that 15 per cent. had 23 presacral segments and 41 per cent had 25.

Variability in ossification is a further predisposing factor in the causation of these anomalies, and they may be all grades of defects, from a complete aplasia of the bone to developmental arrests at any state of the process or merely a delay in attaining a normal appearance. Finck, in 46 autopsies on infants from 2 to 8 weeks old, found that normally there is no fat deposit in the epidural space and in 11 cases noted laminal defects which were covered by the *membrana reuniens posterior*.

Among the most important structures in the causation of abnormalities seen with spina bifida occulta, principally the embryonic tissues of that region which are destined to become fibrous tissue, fat, muscle and bone have to be considered, and the greatest variability is in the bony tissue.

The work of Ernst on malformations of the central nervous system explains many of the changes which affect the lower portion of the spinal cord, and which are considered to be the outstanding defect responsible for neurological symptoms. He refuses to accept the possibility that mesodermal structures (bones, muscles) play any part in the development of the spina bifida and

justifies his attitude by stating that the closure of the medullary groove precedes the formation of the vertebral arches, so that the blastema for the spinal canal must adjust itself to the medullary canal, and not the reverse. The extensive defects which he described are in marked contrast to the appearance of the spinal cord in spina bifida occulta, and though they may produce similar symptoms, in their milder forms, it is necessary to differentiate the 2 types of lesions with respect to their developmental features. In 1909, Fuchs expressed the belief that many syndromes could be explained by assuming an hypoplasia or dysplasia of certain portions of the spinal cord, and this has marked the beginning of the doctrine of myelodysplasia. However, this has never been proved morphologically.

Spina bifida occulta is sometimes associated with external manifestations of the skin over the cleft, such as hypertrichosis, pigmentation, scars or retraction. Peripheral phenomena and visceral disturbances have been seen with spina bifida occulta and its relationship to low back pain has been of great interest. Congenital club-foot was noted to occur in cases where the spinal cord had been elongated by adhesions between a subcutaneous fibrolipoma and the meninges. Hollow-foot or claw-foot in relation to spina bifida occulta was found in 60 per cent of cases by Hackenbroch. X-ray verification of the spina bifida occulta in this group is possible. Bilateral paralysis of the peronei has been found by Hoelen. At operation a mass of fat and connective tissue was found to protrude into the spinal canal through the opening of the spina bifida occulta. Spiller has reported several instances of spina bifida occulta with atrophy and disturbances of the

lower extremities Lucke calls attention to congenital dislocation of the hip in the presence of spina bifida occulta. The appearance of trophic ulcers, resistant to treatment, has been noticed in conjunction with these defects, which occur on the plantar surface of the foot, involving not only the skin and subcutaneous tissues, but also the bones, especially the metatarsals.

Sensory disturbances have been noted in 84 per cent. of cases by Finck, who found anesthesia of the plantar surface of the foot. Visceral disturbances, especially enuresis and nocturia have been frequently observed. Leri performed operations on 24 patients with enuresis and found a fibrous band in every case compressing the dural sac and nerves of the cauda equina.

The *treatment* advocated depends upon the severity of the symptoms. Laminectomy with removal of the fibrous bands and fatty tissue accumulations, has been associated with definite relief in a large number of cases. On the other hand, without paralysis or pain, the seriousness of such an operation does not warrant its use unless some neurological defect exists. The importance of the presence of these spinal clefts as related to many neurological defects of the lower extremity warrants a careful study of the patient by x-ray and direct examination to disclose the presence of spina bifida occulta.

**SPINAL ANESTHESIA.** See ANESTHESIA, SPINAL.

**SPLEEN, RUPTURE OF.** See ABDOMINAL INJURIES

**SPLENECTOMY. — INDICATIONS.**—H. Thursfield (Proc. Roy. Soc. Med. 22. 1493, 1929) has reviewed

the present knowledge concerning the physiology of the spleen. The spleen is a blood reservoir contracting and dilating with the demands of the abdominal viscera, and is enlarged in nearly all acute infections. It is usually not the only splenic tissue in the abdominal cavity, there being, in addition, spleniculi elsewhere, or splenic tissue in the omentum. Removal of the spleen experimentally, or for trauma or cystic disease, results in no permanent change except a decrease in the fragility of the red blood corpuscles. There are 3 clinical conditions in which splenectomy is employed as a routine practice, *ic*, splenic anemia, acholuric jaundice, and the chronic type of recurrent purpura. While many other conditions have been treated by splenectomy, the results in these have not been uniform or successful enough to warrant the operation as a routine procedure.

**RESULTS.**—H. Godard and C. Palios (Rev. de chir., Paris 50. 63 (Feb.) 1931) have done research work on the humoral function of the spleen and made some surgical deductions. Their experience convinces them of the seriousness of splenectomy and the existence of a secretion which is directly due to the spleen, whose suppression leads to general disorders and particularly postoperative anemia. This humoral action probably depends on the physiology of the splenic reticulo-endothelial system, which explains at the same time the intensity of this phenomenon and the relative ease with which the humoral function is replaced.

Muhlbradt (Deutsche Ztschr. f. Chir. 228. 365, 1930) states that experiments have shown that extirpation of the spleen, whether diseased or not, does not affect the bodily economy unfavorably. Furthermore, certain conditions

call for its removal. It is not only indicated, but urgent, even if only temporary improvement follows such removal. Splenectomy has a stimulating effect on the bone-marrow, and the result may have an extremely good effect on the course of the primary disease for which the spleen was removed.

**PREGNANCY FOLLOWING SPLENECTOMY.**—Splenectomy has not been practiced long enough to receive much consideration with regard to subsequent pregnancy. The replies to a questionnaire sent to a group of women who were subjected to splenectomy at The Mayo Clinic by R. D. Mussey and G. G. Burkley (M. Clin. North America 13:1455 (May) 1930) showed that after the operation 23 of the women had 32 pregnancies, with the birth of 28 living children, 2 miscarriages, and 2 premature labors. The course of pregnancy, labor, and puerperium in this group did not show any appreciably greater departure from the normal than that of an average group of obstetrical cases. Pregnancy was followed by recurrence of symptoms only in a case of Banti's disease, in which gastric hemorrhages had occurred prior to removal of the spleen and once during the pregnancy.

There seems to be slightly more than the normal hazard for the fetus, but this appears to be due to the disease for which the splenectomy was done, rather than to the removal of the spleen. In the 32 pregnancies there were 4 fetal deaths. Two babies died in the first year of life, and 1 child required splenectomy for hemolytic jaundice at the age of 7 years. On account of the familial tendency to the development of hemolytic jaundice, a test of the fragility of the erythrocytes should be made in the case of every child born to a parent with hemolytic jaundice.

With regard to the safety of pregnancy after removal of the spleen, on account of severe gastric hemorrhages, the authors report that of 8 cases of splenic anemia, including 1 case in which the condition had advanced to the stage of Banti's disease, severe gastric hemorrhages occurred prior to pregnancy in 4, and in 2 of these hemorrhages occurred during pregnancy. They state that injury to the liver, which may be present in this condition and in Gaucher's disease, may add to the hazard of pregnancy and that any such hazard is probably due to the disease for which the spleen was removed rather than to absence of the spleen. In purpura hemorrhagica, removal of the spleen seems greatly to decrease the hazard of pregnancy.

**SPLENIC EXTRACT.** See ANIMAL EXTRACTS.

**STERILITY, FUNCTIONAL.**—**ETIOLOGY.**—Ovarian hypofunction, either primary or secondary to pituitary or thyroid deficiency, may result in functional sterility. In these patients there is an absence of a demonstrable quantity of female sex hormone in the blood, and absence of the premenstrual endometrium a day or 2 before the expected flow. In a study of 103 patients with functional sterility, C. Mazer and I. Andrussier, (Am. J. Obst. and Gynec. 22:46 (July) 1931) encountered 37 women of this type who, however, menstruated regularly. These women were subjected to a uterine curettage 1 or 2 days before the onset of the expected flow. Only 17 showed a perfectly normal premenstrual endometrium, 4, a premenstrual endometrium with local hyperplasia, 1, an atrophic endometrium; 5, a hyperplastic endometrium, and 10, an interval endo-



metrium Of the 20 showing an abnormal endometrium, only 3 showed a demonstrable quantity of female sex hormone in the blood 1 or 2 days before the period

Hostility of the cervical secretions is indicated when dead spermatozoa are found in the cervical secretions 6 or 8 hours after coitus in women free from endocervicitis, although there are normal sperms in the condom specimen This hostility is probably of endocrine origin and precludes fertility

**DIAGNOSIS.**—Mazer and Andrusier (*loc cit*) attach great value to the Frank and Goldberger test for the blood level of female sex hormone in the diagnosis of functional sterility in regularly menstruating women

A demonstrable quantity of anterior pituitary sex hormone is not obtained in normal fertile women or those with primary pituitary hypofunction Its recovery from the blood of women with functional sterility is pathognomonic, therefore, of primary ovarian hypofunction

**Frank-Goldberger Blood Test.**—At the scientific exhibit of the American Medical Association, June, 1931, P B

last mentioned suggested a method of function It is of great value in the diagnosis of functional sterility in regularly menstruating women Mazer claims that the results are more uniform when a duplicate test is performed simultaneously

The greatest concentration of female sex hormone in the blood is present a day or 2 before the onset of the menstrual flow, according to R T Frank and M A Goldberger (J A M A 94 1197 (Apr 19) 1930)

At this phase of the cycle, 94 per cent of normal fertile women show a demonstrable quantity of the hormone if the test is performed in duplicate Only 39 per cent of regularly menstruating sterile women without pelvic pathology show a positive reaction, hence this test is of value in the diagnosis of functional sterility in women belonging to the latter class A premenstrual curettage in these patients often shows the lack of endometrial development, pointing to defective luteinization Mazer, in the following table, indicates the relationship between the condition of the endometrium and the level of female sex hormone

Premenstrual Endometrial Findings	Female Sex Hormone Level			
	Normal	Threshold	Negative	Total
Interval endometrium	0	1	11	12
Hyperplasia	1	2	5	8
Premenstrual endometrium with local hyperplasia	0	0	4	4
Premenstrual	6	6	5	17
Total	7	9	25	41

Bland, C. Mazer, Arthur First and P Roeder attached great importance to this test, which is an accurate and practical test to determine the level of ovarian activity, almost comparable with the

**TREATMENT.**—In the treatment of functional menstrual disturbances, prophylaxis in the adolescent youth is of utmost importance C H. Lawrence (J A M A 95 1148 (Oct 18) 1930)

found that 14 per cent of functionally sterile women gave a history of adolescent disturbances of endocrine function which resulted in incomplete development of the genital organs

**Foci of infection** should be removed and a **balanced diet**, with sufficient quantity of proteins and vitamins A and E containing foods, should be prescribed. In the administration of endocrine products, the physiology of the ovary and pituitary gland must be borne in mind. **Female sex hormone** causes an increase in growth and vascularity of the uterus, and renders it, therefore, more responsive to ovarian stimulation. Theoretically, it is best given combined with injections of the **corpus luteum hormone**.

Orally, female sex hormone is one-fifth as potent as when administered subcutaneously. When given in divided doses over a 24-hour period, it is not rapidly eliminated through the urine, and is, therefore, better able to concentrate in the uterine mucosa. The oral administration is efficacious because of the marked stability of the hormone to strong bases, acids and artificial digestion. J. A. Morrell, H. H. Powers, J. R. Varley and J. De Frates (*Endocrinology* 14:174 (May-June) 1930) have shown that the oral administration of female sex hormone in quantities 5 times that of the hypodermic dose produces artificial menstruation in spayed monkeys.

The available standardized commercial products of female sex hormone unfortunately lose their strength very quickly. Among the products at present available may be mentioned **estrogen**, **amniotin**, **plestrin**, **progynon**, **menformon** and **theelin**. The latter is an aqueous solution of the pure crystalline hormone.

Injections of **corpus luteum hor-**

**mone** are advised for regularly menstruating sterile women who fail to show a premenstrual endometrium 1 or 2 days previous to the expected period. This is preferably given during the latter third of the menstrual cycle, 2 ampules of aqueous extract of **corpora lutea** from pregnant cattle being given daily for 10 days.

C. Mazer reports better results with **x-ray stimulation of the ovaries** and **pituitary gland** than with any other form of treatment. Six of 38 sterile women with menstrual derangement thus treated were delivered of healthy offspring, 19, or 50 per cent, are menstruating regularly and 7 show marked improvement. In cases of primary ovarian failure with compensatory hyperfunction of the anterior pituitary gland, irradiation of this gland is probably harmful.

**STERILIZATION OF WOMEN.**—Various methods have been recommended for the *temporary sterilization* of women. In regard to the surgical methods, H. Naujoks (*Zentralbl f Gynak* 55:81 (Jan 10) 1931) considers that the term reversible sterilization should be used in preference to temporary sterilization.

Sterilization by irradiation is inadvisable, because the correct dosage as well as the duration of the sterility cannot be predetermined.

Naujoks advocates a procedure which is a modification of Madlener's method. Madlener crushes the tubes for permanent sterilization. The author modifies this method by crushing the tube, not in the middle but near the infundibulum. After the tube is crushed with a Roux's enterotripter, 2 silk threads are passed through the mesosalpinx and they are tightly fastened around the tube at the

ends of the crushing furrow. Care should be exercised that the wall of the tube is not cut with the thread. This method, he claims, is more reliable than burying of the tube or ovary, and possesses the advantage of easy reversibility, which is done by the simple excision of the ampulla with the diathermy knife.

**STOMACH, DISEASES OF.—**  
**DIAGNOSIS.—Subacidity.**—Achlorhydria and achylia gastrica have received considerable attention in recent literature.

J. F. Wilkinson and T. H. Oliver (Lancet 1 66 (Jan 10) 1931) analyzed 100 cases of conditions frequently associated with achlorhydria which they divided into 5 groups, depending upon the associated symptoms. The *first group* included 53 patients with gastrointestinal disturbances such as diarrhea, flatulence, and neurasthenia. Twenty-five had achylia and 18 hypoacidity. Histamine was not used as a gastric secretory stimulant. In the *second group* were placed 25 patients with sore tongue or ulcerative stomatitis, with or without the above gastrointestinal symptoms. Of this number, 9 had achylia, 6 hypoacidity, 7 normal acidity, and 3 hyperacidity. Five patients with skin lesions and gastrointestinal symptoms were placed in *group three*. There was only 1 case of urticaria and angioneurotic edema. In this group achylia was found in 4 cases, hyperacidity in 1, and hypoacidity in 1.

In the *fourth group* were placed 5 patients with rheumatoid arthritis. One had diarrhea which was associated with hyperacidity, 4 had glossitis, 3 showing achylia and 1 hypoacidity.

Ten cases of debility and secondary anemia composed the *fifth group*. Four had achylia and 4 hypoacidity.

Of the entire group, 45 cases showed achylia by the methods used by these authors, and an additional 31 had hypochlorhydria, giving a total incidence of 26 per cent of subnormal acidity in the clinical conditions studied.

One hundred cases of achlorhydria, as judged by the usual fractional gastric analysis, have been presented by L. H. Hitzrot (M. Clin. North America 14: 1025 (Jan) 1931). Histamine was used in 47 cases. Carcinoma of the stomach was diagnosed in 23 per cent, chronic gastritis in 17 per cent, biliary disease in 11 per cent, and primary anemia in 4 per cent. Focal infection was the only associated abnormality in 14 per cent, while neurosis was the chief diagnosis in 10 per cent. The highest incidence was found in the fifth and sixth decade, 48 per cent of cases being between 40 and 60 years of age.

F. R. Vanzant (Proc. Staff Meet. Mayo Clinic 6:297 (May 20) 1931) analyzed a large series of cases at The Mayo Clinic. In a review of 3381 gastric analyses performed on patients with apparently normal gastrointestinal tracts, it was found that the incidence of achlorhydria increased from 4 per cent at 20 years, to 26 per cent at 60 years. Achlorhydria was present in 12.1 per cent of the entire series, 10.8 per cent of males and 13.8 per cent of females.

Studying the incidence of achlorhydria in blood relatives of primary pernicious anemia patients, Connor found that 15.7 per cent of those under 40 years of age, and 42.3 per cent of those over 40 years had this abnormality, a distinct increase over F. R. Vanzant's figures (Proc. Staff Meet. Mayo Clinic 4:200 (June 26) 1929).

W. B. Castle, C. W. Heath, and M. B. Strauss (Am. J. M. Sc. 182:741 (Dec.) 1931) have cited evidence that

achylia is not essential in the diagnosis of Addisonian anemia. These authors contend that the development of pernicious anemia is dependent upon the absence of an intrinsic factor in gastric juice. This factor is independent of gastric acid and enzyme secretion, although it is most often absent in achylia. Two cases with normal gastric secretion of acid and enzymes, but lacking the antianemia factor, are presented in detail by these writers.

*Clinical Methods of Determining Gastric Acidity*—M. J. Matzner and I. Gray (Arch. Int. Med. 47: 58 (Jan.) 1931) have pointed out various faults in all the usual methods of gastric analysis, especially in cases of subtotal gastrectomy. They suggested the use of histamine as a gastric stimulant and determination of the urinary alkaline tide as an estimate of gastric secretion. This work was based upon the previous observations of R. S. Hubbard, S. A. Munford and E. G. Allen (Am. J. Physiol. 68: 207 (Apr.) 1924) and D. T. Davies (Brit. J. Exper. Path. 10: 1 (Feb.) 1929), who found that persons with normal gastric acidity had less acid in the urine after meals, while no such change was noted in those with achlorhydria. F. D. Ackman (Canad. M. A. J. 15: 1099 (Nov.) 1925), using histamine as a stimulant, found a definite alkaline tide in normals but none in cases of achylia.

M. J. Matzner and I. Gray (Arch. Int. Med. 47: 202 (Feb.) 1931) were able to demonstrate an alkaline tide in only 50 per cent of those patients secreting hydrochloric acid after histamine. More constant results were obtained using bouillon as a gastric stimulant. In the group so studied an alkaline tide was found in 85 per cent of those having acid secretion. Accord-

ing to M. J. Matzner, I. Gray and H. Greenfield (Arch. Int. Med. 47: 421 (Mar.) 1931), one suggested source of error is that in patients with continuous hypersecretion (Reichmann's disease) a definite alkaline tide fails to appear.

R. S. Hubbard (Arch. Int. Med. 46: 994 (Dec.) 1930) presented the results of 365 tests on 296 patients, using a test breakfast of toast, butter, glass of milk, an egg and a glass of water. Six specimens of urine were collected at hourly intervals after the test meal and the *pH* immediately determined. An alkaline tide was said to be present if the *pH* immediately determined. An specimen or by 0.5 in any two.

This writer found that about 80 per cent of patients not showing an alkaline tide had either achlorhydria or marked hypochlorhydria. No distinction was possible between normal and hyperacid secretion. The presence of an alkaline tide was said to indicate "almost always" the presence of acid in the gastric juice.

**CHRONIC GASTRITIS.**—Chronic gastritis may result from a number of causes, including acute gastritis from food poisoning or acute infection, excessive consumption of alcohol, use of indigestible food, or from swallowing infective material from the nose and throat. It can be diagnosed only by means of a fractional test meal, which shows excessive mucus in most or all of the fractions as well as in the fasting juice. The mucus not only blocks the mouths of the gastric glands, but also neutralizes free acid. Consequently, achlorhydria is frequently present. A. F. Hurst (Clin. J. 60: 97 (Mar. 4); 109 (Mar. 11) 1931) does not believe that administration of hydrochloric acid in these cases is usually necessary, since he has found that preliminary lavage followed by a second test meal often

reveals a normal acid secretion. In some cases daily lavage over a varying period is necessary before acid is obtained. Hydrogen peroxide, beginning with 2 cc ( $1\frac{1}{2}$  dram) to the pint (500 cc), aids in removal of the mucus. Later, 15 cc ( $1\frac{1}{2}$  ounce) to the pint (500 cc) can be used. The number of lavages at each sitting depends upon the amount of mucus obtained, washing being continued until the return is clear.

**GASTRIC ULCER.—Treatment.**—Unsuccessful results in the treatment of ulcer in the past were frequently due to lack of adequate knowledge of its pathogenesis, to lack of persistent treatment, and to lack of the realization that even when an ulcer healed, the ulcer diathesis remained, according to A. F. Hurst (Clin J 60 97 (Mar 4), 109 (Mar 11) 1931). The first principle of treatment suggested by this writer is attention to the acid factor. The presence of free hydrochloric acid is required for the development of an ulcer. A diet must, therefore, be chosen which produces as little secretion of acid as possible, atropine and olive oil should be given to inhibit the secretion of acid, and alkalis to neutralize the acid when it has been secreted during the day. The diet must also be nonirritating and must be adequate to maintain nutrition. Hurst deprecates the use of standard diets in all ulcer patients. He believes that when a diet has been chosen to suit the special requirements of an individual, no further change should be made until the ulcer has completely healed. It has been found that milk is an effective neutralizer of gastric acid, the administration of small quantities, at hourly intervals, tending to produce complete achlorhydria for a considerable part of the day.

Since an infective factor is the essen-

tial etiological cause of gastric and duodenal ulcer, according to this author, pyloric and antral abscesses, infected tonsils and sinus infection should be appropriately treated. Accessory factors of importance are the use of tobacco, fatigue and exposure, all of which should be avoided, especially during the period of strict treatment.

Strict treatment must be continued until the ulcer has completely healed. The spontaneous pain often disappears within 24 hours, and it rarely lasts for more than a week. Deep tenderness and rigidity may continue for a longer period, but they generally disappear long before healing is complete. The stools should be tested twice weekly for occult blood until 3 consecutive tests give a negative reaction. If evidence of bleeding continues even after disappearance of symptoms in specimens of feces obtained in such a way as to rule out hemorrhoidal bleeding, early malignancy should be suspected, according to Hurst. An x-ray examination should be made weekly until the crater has disappeared. This criterion is usually impossible to establish in duodenal ulcer, where the actual niche is frequently not seen. Strict treatment in any case should cover a period of at least 4 weeks and large chronic ulcers may take as long as 3 months.

The *after-treatment* in ulcer cases is extremely important. Hurst's (*loc cit*) investigations have clearly shown that "the tendency to recurrence after medical treatment, and of the equal tendency to the development of new ulcers in the stomach, duodenum or jejunum after surgical treatment, are primarily the result of constitutional peculiarities of the individual." If the patient returns to the conditions existing previous to the development of the ulcer, the

chances are great that he will have recurrences. This can be prevented, according to this writer, only if, in addition to the removal of all foci of infection, he is given instructions as to his diet and habits, which he must obey for the rest of his life. Such instructions should include a diet consisting only of foods which can be reduced to a fluid condition by chewing. No raw fruits or vegetables, no pickles, and no cooked vegetables except in the form of purées, are allowed. Any chemical irritant must also be forbidden; this includes alcohol, strong tea or coffee, and many drugs. Smoking must be reduced to a minimum.

Several series of experiments with various alkalis have been done under Hurst's supervision. It was found that when an excess of alkali was added to a constant amount of 0.3 per cent hydrochloric acid, the pH values varied with the alkali used. Magnesium oxide and sodium bicarbonate produced an alkaline solution, reaching its maximum within a minute. The value for magnesium oxide was 10 and for sodium bicarbonate 8. Magnesium carbonate solution reached a maximum of 8.5 in 2 minutes. Solutions of sodium and potassium citrates and tribasic calcium and magnesium phosphates attain neutrality (pH 7.0) within a minute but never become alkaline, while bismuth subcarbonate and aluminum silicate and hydrochloride do not reach a final pH above 4.0. Further experiments using a fixed quantity of alkali (2 Gm—30 grains) with varying amounts of 0.3 per cent hydrochloric acid showed that, weight for weight, magnesium oxide is the most efficient alkali and that bismuth subcarbonate is the least. Calcium carbonate, sodium and potassium citrates, and tribasic calcium and magnesium phosphates have less than one-fifth the

neutralizing power of the same weight of magnesium oxide, while sodium bicarbonate has about one-quarter the power. It has been shown by Crohn that sodium bicarbonate and magnesium oxide, after neutralizing the acid present in the stomach, stimulate secretion, being the most powerful gastric stimulants known excepting histamine. However, it has further been shown that when alkalis are given in doses insufficient to render the gastric juice alkaline, such stimulation of secretion does not occur.

Hurst believes that calcium carbonate is an almost ideal alkali for the treatment of ulcer, for although it has only two-thirds of the neutralizing power of sodium bicarbonate, it does not give rise to secondary hypersecretion. He also points out the value of combining sodium or potassium citrates with milk, preventing the immediate coagulation of rennin and combining the neutralizing effect of milk with that of citrate.

Regarding the question of *alkalosis*, Hurst (*loc cit*) points out that the symptoms seem to be dependent upon chloride depletion in the body. The danger of alkalosis developing in ulcer patients can be markedly reduced by the addition of salt to the diet.

The following diet is suggested by this author:

1 Five ounces (150 cc) of milk every alternate hour from 8 A.M. to 10 P.M.

2 Every other hour, alternating with the above, a 5-ounce (150 cc) feeding made up of (a) cream of wheat, junket, custard, arrowroot; to any of these may be added fruit jelly.

(b) At least 2 feedings should consist of a thick soup or purée of potato, artichoke, cauliflower, or parsnip.



3 A cracker with butter should be eaten with 3 feedings. Small amounts of water may be drunk between feedings. One-half ounce (15 cc) of strained orange juice should be taken with one of the drinks.

4 One ounce (30 cc) of cream should be added to the 11 A M, 1 P M, and 5 P M feedings.

5 One dram (4 cc) of mixture No 1 should be added to each milk feeding and 1 or more drams of milk of magnesia, according to the condition of the bowels, should be taken before these feedings.

6 One dram (4 cc) of mixture No 2 should be taken before the 8 A M and 3 P M feedings and 2 drams (8 cc) before the 10 P M feeding.

7 One-half to 1 dram (2 to 4 cc) of prepared chalk should be given halfway between feedings.

8 At 7 A M  $\frac{1}{2}$  ounce (15 Gm) of bismuth subcarbonate or powdered charcoal washed down by 5 ounces (150 cc) of water.

#### Mixture No 1

R *Sodu citratis* gr xv (1 Gm).  
*Aqua* ad 5j (4 cc).

#### Mixture No 2

R *Atropina sulphatis* gr  $\frac{1}{200}$  (0.0003 Gm)  
*Aqua* ad 5j (4 cc)

*Pyloric obstruction*, according to Hurst (*loc. cit.*), rarely develops during treatment. It is usually the result of many years of alternating activity and partial healing. Many authors advise gastroenterostomy when enough obstruction is present to produce 6-hour retention by x-ray. In Hurst's experience, however, it is possible for obstruction to disappear under medical treatment, even though there had been 12 or even 24-hour retention before treatment was instituted.

## GASTRODUODENAL ULCER.

—*Surgical Treatment*.—C Bolton (Brit M J 1 727 (Apr 19) 1930), discusses the treatment of gastric and duodenal ulcer and draws the following conclusions:

1. Gastric and duodenal ulcers are primarily medical diseases.

2. The majority of ulcers will heal under medical treatment if the treatment is begun at an early stage of the malady.

3. For the rest of his life the patient must obey the dietetic and other rules laid down for him after the conclusion of treatment, otherwise he is liable to a relapse, especially if the treatment was not employed at a comparatively early stage of the disease.

4. An uncomplicated ulcer should not be subjected to operation until it has been proved incurable by medical treatment.

5. If the lesion is proved incurable by medical treatment, as regards either healing or recurrence, operation is indicated.

6. In addition to healing or removing the ulcer, surgery is expected so to alter the gastric mechanism that recurrence is impossible, but as this result is at present uncertain, the gastric contents should be examined after every operation and unless achlorhydria is established, the patient should be referred back to the physician for medical treatment.

7. More attention should be paid by physicians to the treatment of dyspepsia and the early diagnosis of ulcer. When the presence of an ulcer is recognized, adequate medical treatment should be instituted at once.

In tracing the trend of treatment of ulcer since 1901, A J Sullivan (New England J. Med. 204:191 (Jan 29) 1931) states that, today, in better clin-

ics, there is close cooperation between the internist and surgeon

The *indications for surgery in gastric ulcer* are (1) perforation, (2) repeated and severe hemorrhage, (3) the possibility of malignancy, (4) hour-glass deformity, (5) pyloric obstruction, (6) absence of healing or the occurrence of only partial healing after thorough medical treatment, and (7) recurrence in spite of thorough medical treatment

The *indications for surgery in duodenal ulcer* are (1) perforation, (2) repeated or severe hemorrhage, (3) pyloric or duodenal obstruction, (4) absence of healing or the occurrence of only partial healing after thorough medical treatment, and (5) the development of a recurrence in spite of thorough medical treatment

*Acute perforation*, whether duodenal or gastric, is an indication for immediate surgical intervention. Early diagnosis and operation are of prime importance. **Simple closure** is considered the procedure of choice in most cases.

In cases of *hemorrhage*, surgery is usually contraindicated when the patient is still bleeding. Rare exceptions to this rule are cited. A patient who presents himself with a bleeding ulcer and gives a history of hemorrhage is not a surgical problem until after thorough medical treatment has failed to cause improvement. If the patient is under medical management when the hemorrhage occurs, surgery is indicated. When possible, the ulcer should be **excised**.

According to J. S. Horsley (Ann Surg 92.545 (Oct) 1930), it seems probable that the vast majority of cases of peptic ulcer can be cured either by medical treatment, consisting largely of regulation of diet, or by **operation**.

After any stomach operation medical treatment, particularly regulation of the diet, should be carried out for at least several months. This is just as essential in a stomach that has been temporarily crippled by the operation, until it can recover its tone and function, as it is to use splints after an accurately set fracture until the bone itself has become strong. The kind of operation done should be suited to the type of lesion present. In a few patients, however, there seems to be an inherent tendency toward *recurrence* of a peptic ulcer even after multiple operations and careful medical treatment. Fortunately, they constitute a small percentage of the total number of patients with peptic ulcer. This group can usually be effectively managed along lines of **rest for the stomach**, such as **feeding by jejunostomy** for months or even permanently, as recommended by Balfour.

**Results of Operation**\*—J. M. T. Finney and E. M. Hanrahan (Ann Surg 92.620 (Oct) 1930) analyze 737 cases of ulcer of stomach and duodenum in which operation was performed. One hundred and ten operations were performed after perforation, with an operative mortality of 23.6 per cent. The mortality in all operations for chronic ulcer was 8.6 per cent. Of the chronic ulcers, 268 were gastric and 339 duodenal. There were 20 operations for postoperative marginal ulcer in the chronic group. The operations included such miscellaneous procedures as excisions, with knife or cautery, wedge and sleeve resections, either with or without a gastroenterostomy, simple gastroenterostomy, pyloroplasty, with or without excision, and partial gastrectomy. The miscellaneous procedures were applied to those cases in which

\* See also Results of Gastric Resection

pyloroplasty or gastroenterostomy were for some reason contraindicated. *Pyloroplasty* was the operation of choice for ulcers of the duodenum, pylorus or antrum, when the ulcer could be included in the pyloroplastic incision and when the duodenum could be satisfactorily mobilized. *Partial gastrectomy* was occasionally used for duodenal ulcer and more commonly for ulcers of the body of the stomach, when conditions warranted the more radical procedure. *Gastroenterostomy* was used for ulcers of the lesser curvature and fundus when partial gastrectomy was not practicable, and for ulcers of the pylorus and duodenum when difficult mobilization or the presence of excessive scar tissue precluded pyloroplasty.

The *operative mortality* for this series approximated that of most hospital series covering similar periods and performed under similar circumstances. The figures by operations are as follows: miscellaneous operations of expediency, 26.9 per cent; gastroenterostomy, 8.1 per cent; pyloroplasty, 5.2 per cent; and partial gastrectomy, 12.9 per cent. The operative mortality in 84 cases of gastroenterostomy in the Johns Hopkins Hospital between 1925 and 1930 was 2.4 per cent. The operative mortality following pyloroplasty for duodenal ulcer was 2.7 per cent. This mortality is satisfactory especially as these operations were done by men of varying experience, from assistants in training to older experienced surgeons.

The *end-results* of these operations also correspond closely to those of most similar series, *i.e.*, 85.6 per cent benefited by the operation. Duodenal ulcer yielded better results than gastric, even after allowance is made for those patients with gastric ulcer known to have died later of carcinoma.

The *recurrence of ulcer* after gastroduodenal ulcer resection has been investigated by F. Starlinger (Arch. f. klin. Chir., 160: 409 (July) 1930). He collected a total of 25,647 cases from 84 large clinics and hospitals—Billroth I, 7789; Billroth I, with end-to-end gastroduodenostomy, 869; Billroth II, with antecolic gastroenterostomy, 138; Billroth II with retrocolic gastroenterostomy, 16,765; Billroth II with Y-anastomosis, 86. In the Billroth I type, there were 0.9 per cent of recurrences by end-to-end anastomosis, 0.3 per cent by end-to-side. In Billroth II type, with antecolic gastroenterostomy, 2.2 per cent and 0.5 per cent if Braun's enteroanastomosis was added. In the Billroth II with Y-anastomosis recurrence was found in 2.3 per cent. Starlinger observes that as recurrence was met with but 169 times in the enormous total, this minimal percentage is no contraindication against excision of large indurated ulcers.

The *causes of failure of resection* for gastric and duodenal ulcers is discussed by H. von Haberer (Zentralbl. f. Chir. 57: 66 (Jan. 11) 1930). The author states that sometimes failure is due to faulty, too extensive resection. It is most frequent after resection for gastritis, including ulcerous gastritis. Resection fails also when it is done on the basis of an erroneous diagnosis. Failure when the operation was definitely indicated may be due to inadequately extensive resection. Both the pylorus and the antrum must be removed. Moreover, as long-standing callous ulcer of the stomach or duodenum is usually complicated by catarrhal changes in the mucosa, dietetic after-treatment should be given for at least 9 months. The author considers these changes amenable to treatment and has found that in cases

in which they are present the results of resection become better with the lapse of time

Technical considerations may constitute an important indication for resection. When a Billroth I anastomosis is too narrow, it causes signs of stenosis and when the jejunal loop in a Billroth II operation is too long, there is stasis. In some cases ulcers may be overlooked, especially in the duodenum. The author's technic is described in detail.

Von Haberer states that in the cases of nervous patients, reoperation is inadvisable, as the prognosis is worse with each operation. He reports a case.

With regard to the *indications for the operation*, von Haberer says that he objects to a time limit, as he has operated with good results in cases in which the lesion was present for less than 3 years and in cases in which it had been present for more than 20 years.

In conclusion, he reviews the incidence and type of *recurrences* after resection in his cases. Of 2310 cases, an operative or roentgenologically demonstrated ulcer recurred in only 15 (0.6 per cent). In all, von Haberer has done 127 transverse resections, 706 Billroth II resections, 1276 Billroth I resections, and 201 Billroth I resections with end-to-side anastomoses. Among these there were 121 radical operations for jejunal ulcer.

According to A. A. Berg (Ann. Surg. 92:340 (Sept) 1930), ulcer of the stomach is the same disease as ulcer of the duodenum and responds to the same methods of treatment. In the chronic stages it can be cured only by surgery.

Three important factors concerned in the formation of a gastric or duodenal ulcer are specific ulcer gastritis, free hydrochloric acid in the stomach, and

secondary infection in the stomach or duodenum.

In chronic ulcer gastritis the symptoms are similar to those of ulcer, but at operation no ulcer is found. In its early stages this condition can be cured by proper medical treatment. When an ulcer is fully developed, medical treatment may alleviate the symptoms, but is rarely curative.

Up to 1920, Berg treated gastric and duodenal ulcer by the usual surgical methods—gastroenterostomy, ulcer excision, cautery puncture, and pyloroplasty. In the follow-up of patients so treated he found that only about 50 per cent were cured and that 30 per cent had developed ulcers at the gastroenteric stoma or a recurrence at the site of the original lesion. These findings were similar to those of a number of Continental surgeons. Accordingly, an operation which would remove the factors responsible for the ulcer was sought. **Subtotal or partial gastrectomy** was found to meet the requirements. This operation consists in the removal of the antrum and part of the body of the stomach, together with the pylorus and the affected part of the duodenum, followed by reestablishment of the connection between the stomach and duodenum or jejunum. After a trial of various technics, a uniform procedure was adopted which has been used since 1923 with routinely good results.

The operation is begun with ligation of the cardiac artery. The desired portion of stomach and duodenum is then removed and a gastrojejunal anastomosis is established according to the method of Hofmeister. In the mobilization of the duodenum great care must be taken to avoid entering the pancreatic capsule. The formation of a hematoma around the head of the pancreas or duo-

denal stump must also be prevented. All raw areas must be carefully covered. Care in the closure of the duodenal stump is necessary to prevent duodenal fistula. If the transverse mesocolon is separated from the posterior wall of the stomach before clamps are applied, the danger of injuring the middle colic artery is eliminated. Hemorrhage from the cut end of the stomach can be prevented only by grasping and tying each blood-vessel in the wall of the stomach separately.

In the period from 1923 to 1929, 405 *primary subtotal gastrectomies* were done with a mortality of 7.9 per cent. (32 deaths). If 4 deaths due to causes not related to the operation are excluded, the mortality was 6.9 per cent.

In comparing the results of primary subtotal gastrectomy with those of gastroenterostomy, the author cites statistics showing that gastroenterostomy had a mortality as high as, or higher than, that of subtotal gastrectomy and was followed much more frequently by recurrence of symptoms and gastrojejunal ulcer.

In 105 secondary subtotal gastrectomies reviewed by the author, the mortality was 20.9 per cent.

In a total of 516 cases in which a primary or secondary subtotal gastrectomy was done the incidence of recurrence was only 1.1 per cent.

From 2 tables of cases treated medically, the author concludes that after medical treatment a lasting cure is rare and the ultimate mortality is considerably higher than in surgically treated cases.

E. S. Judd and M. E. Hazeltine (Ann. Surg. 92:563 (Oct.) 1930) report on the *local operations* which have been performed for duodenal ulcer at The Mayo Clinic. The first local oper-

ation in the Clinic for ulcer of the duodenum was a Hemecke-Mikulicz operation performed in 1896, and the first operation for excision of ulcer of the duodenum was done in 1902.

**Gastroenterostomy** will probably remain the popular operation for duodenal ulcer. It is satisfactory in all cases except in those in which secondary ulcers develop and those in which hemorrhage occurs and the bleeding may continue.

The operation of **excision** was developed to prevent jejunal ulcer and to reduce the incidence of bleeding after gastroenterostomy for hemorrhagic ulcer.

For many years the local operation consisted in excision of the ulcer or destruction of the ulcer by cautery with simple closure of the area in the duodenum. Of late, it has been thought that removal of the anterior part of the pyloric sphincter in addition to excision of the ulcer results in more complete relief of the symptoms. With this removal of muscle, everything is accomplished that gastroenterostomy can accomplish, and, in addition, the ulcer is removed.

In cases in which multiple ulcers are encountered and the removal of all of them is impossible, it is probably best to remove the anterior ulcer, close the opening in the duodenum, and then complete the operation with gastroenterostomy.

The local operation is limited to cases in which the duodenum is fairly mobile. However, with increasing experience in these cases, the surgeon comes to realize more and more that it is not so difficult to mobilize a duodenum which is fairly well fixed and that this should be done in cases in which excision of the ulcer is definitely indicated.

Gastroenterostomy is particularly satisfactory for older patients, especially if obstructive symptoms have developed. It is less satisfactory in young patients.

A study of the immediate results of the local operation shows that it can be done with very little risk. In the 1363 cases covered by this report the mortality was 0.44 per cent.

The ultimate results in this group of cases are practically the same as the ultimate results obtained by gastroenterostomy, 90 per cent of the patients from whom detailed reports have been received obtained satisfactory relief.

The local operation can be performed in about 50 per cent of cases of duodenal ulcer, and in these it will probably give better immediate and ultimate results than gastroenterostomy.

Five hundred consecutive cases of duodenal ulcer in which gastroenterostomy alone was done were studied by D. C. Balfour (Ann Surg 92:558 (Oct) 1930). From the standpoint of relief of symptoms, it was found that after operation 87 per cent of the patients obtained relief which they had been unable to obtain by any other means. In 69 per cent either the relief had been so complete that the patient had paid no attention to diet or to habits of living, or dyspepsia was so slight as to be readily controlled by simple measures. In 18 per cent the results could be classified as fair. In 13 per cent the patients did not obtain permanent relief from operation. The deaths within 5 years from all causes were 21 (4.28 per cent). In no case in the series, or in any other series studied, did perforation of the duodenal ulcer, either acute or subacute, occur after gastroenterostomy had been done. In other words, satisfactory gastroenterostomy apparently afforded absolute protection

against this serious complication. In none of the cases in this group did obstruction of the pylorus develop following gastroenterostomy. Forty-five of the 500 patients (9 per cent) had one or more hemorrhages after operation, but only 1 of the 500 died from hemorrhage. The study also confirmed the fact that such hemorrhages often are directly associated with unusual physical and mental strain, overloading the stomach, excessive use of tobacco and alcohol, and gross dietetic indiscretions and severe focal infection.

No instance of carcinoma developing subsequent to operation was encountered. The protection afforded by gastroenterostomy against the formation of a secondary chronic ulcer is approximately 96 per cent. Twenty patients had recurrent ulceration (4.07 per cent of 491 cases), and of these, gastrojejunal or jejunal ulcer was listed in 16 cases, a total percentage of 3.25 occurring in a period of 10 years or more after operation.

One hundred cases were studied in which gastroenterostomy alone was done for gastric ulcer. The operative mortality in this series was 3 per cent. Seventy-nine per cent of the patients 5 years or more after operation, were relieved. In 50 per cent the relief had been complete; in 29 per cent slight and easily controlled symptoms occasionally occurred, the patient considering the results of operation as good. In 4 per cent the result was classified as fair, in 17 per cent the result was poor.

Gastroenterostomy affords almost complete protection against the complications of perforation and obstruction. The subsequent deaths from all causes in this group during 5 years after operation were 17. The protection against recurrence or reactivation



of ulcer afforded by gastroenterostomy alone for gastric ulcer is approximately 96.9 per cent.

It is a significant fact that gastrojejunal ulcer is not a problem in the treatment of gastric ulcer since the complication did not occur in this group. In cases in which the operation of choice, namely, excision and gastroenterostomy, is possible, gastrojejunal ulceration is almost unknown.

The striking fact in the study of this series of 100 cases is that an indirect operation alone for gastric ulcer can be depended on to give a high percentage of good results in cases in which the removal of the lesion, by any method, is difficult, and partial gastrectomy is associated with prohibitive operative risk and an unwarranted sacrifice of the stomach.

E. E. Larson (California and West Med 32:183 (Mar.) 1930) reports the case of a man, aged 41, on whom a posterior, retrocolic, retroperistaltic, short loop gastroenterostomy was done for duodenal ulcer. Forty-one days after an uninterrupted recovery, the patient was seized by an excruciating pain in the epigastrium, followed by copious vomiting which contained no blood. There was noted a fulness in the upper left abdominal quadrant. A diagnosis of intestinal obstruction incident to the gastroenterostomy was made. At operation it was found that no adhesions existed between the former operative scar and the viscera. The mass in the left upper quadrant consisted of *edematous loops of jejunum and ileum* which had become *strangulated* following migration through the artificial aperture always resultant on gastroenterostomy, the boundaries being the ligament of Treitz, the mesocolon, the stomach and the anastomosis. The loops were easily

pulled back through the stoma and replaced in their normal position. No injury was done to the anastomosis. Four interrupted chromic catgut sutures were then used to close the opening. The patient made an uneventful recovery and has remained well.

**Treatment of Hemorrhage.**—(Peco (Semana med 1:429 (Feb. 13) 1930) observed 34 cases of hemorrhage caused by gastric and duodenal ulcers, in 17 of which the hemorrhages were profuse. The mortality among the entire group of 34 patients was 3 per cent, in the group of 17 with grave hemorrhages, 6 per cent. The author advises medical treatment at the time of hemorrhage. After the first large hemorrhage disappears, if the symptoms suggest healing of the ulcers, operation is not performed, with 2 exceptions: (1) if the symptoms of ulcer reappear, and (2) if the hemorrhage recurs. If the hemorrhage is of a persistent type and the patient is in good general condition, the intervention should be made without delay, preceded by **transfusion**. **Operation** is indicated also in patients with ulcer who have small and repeated or minimal and continuous hemorrhages, or when occult blood is constant. In bleeding ulcers the best treatment is **resection**, though its performance sometimes is not possible. In 33 cases the author was able to perform resection in only 5 instances. Ligation of the vessels along the borders of the ulcer and gastroenterostomy do not stop the hemorrhages. The author considers that the ideal treatment should be immediate operation after a hemorrhage, followed by resection of the ulcer.

O. Kingreen (Zentralbl f Chir. 57:1141 (May 10) 1930) warns against attempting palliative measures when a

gastric ulcer bleeds because, he says, it is never certain whether the first bleeding will be the only one. Transfusions of blood and saline solutions are not to be relied on, as was shown in 1 case cited. **Operation** affords the only certain chance of saving the patient's life. If the bleeding is sufficiently severe to call for **blood transfusion**, this should be followed immediately by an operation.

**Treatment of Acute Perforation.**

—According to A. G. Bryce (Brit. M. J. 1 774 (Apr. 26) 1930), in 125 cases of acute gastric or duodenal perforation in which suture without gastroenterostomy was performed within 12 hours after the perforation, the immediate mortality was 9.6 per cent, and in 26 cases in which the operation was performed more than 12 hours after the perforation it was 26.9 per cent.

In a follow-up made 2 years later, 32 per cent of the patients stated that they were entirely free from gastric disturbances.

The immediate results after suture alone in pyloric and duodenal perforations are practically identical. Secondary operation is more frequently indicated in pyloric perforations.

Closure must be safe. In exceptional cases, safety may demand something more radical than mere suture, with or without gastroenterostomy. When more radical procedures are not justified, careful apposition of the edges of the perforation by suture with reinforcement of the suture line by an omental graft is preferable to the infolding of a wide area of stomach wall.

Gastroenterostomy should usually be reserved for cases in which stenosis has already developed or is apt to result from healing. The presence of an unnecessary gastroenterostomy is not with-

out risk. The systematic performance of gastroenterostomy at the time of perforation without a definite indication is not likely to diminish the mortality.

In discussing the incidence of *hemorrhage* in perforated gastroduodenal ulcers M. Behrend (J. A. M. A. 95 1889 (Dec. 20) 1930) states that the perforative type is more common than the bleeding one. In a year he operated on 24 perforations but did not observe a single bleeder. The indurated, punched-out ulcer has firm edges, it does not bleed because the vessels have been partially obliterated by the hard connective tissue. They may perforate, depending again on the thickness of the base of the ulcer. The bleeding ulcer is usually acute; hence the area affected is much smaller in extent. The edges of these ulcers are soft, with rounded borders; the surrounding mucosa is congested and it often becomes difficult to locate the bleeding unless the suspected viscus is opened. Even then, the source may not be located. In perforated ulcer usually there is found a solution of continuity in the center of an indurated wall of stomach or duodenum. (The same is true of perforations without previous gastric symptoms.) Another rare type of perforation is found when the wall surrounding the ulcer is perfectly flaccid with little or no inflammatory reaction.

The histologic picture of the ulcers described can be verified under the microscope; *e.g.*, in the chronic type the base shows a few small vessels. They have been pressed on by the proliferation of fibrous tissue. As a consequence, these do not bleed as readily as the acute or subacute type. In these there is very little inflammatory reaction, with almost an entire absence of connective tissue elements. The ves-

sels, therefore, have not been compressed because of the absence of scar tissue, as in chronic ulcer. Also in the acute and subacute forms the capillaries are large, which naturally predisposes to hemorrhage. The fact that bleeding ulcers rarely perforate and perforated ulcers rarely bleed may be explained anatomically, there is a bloodless area around the pylorus responsible for some of these deductions, physiologically, the exuding juices prevent hemorrhage, while pathologically, the age of ulcer determines bleeding or not.

From an investigation of the results of various operative methods in perforated gastric ulcers, R. Muhsam (Deutsche med Wchnschr 56 346 (Feb 28) 1930) comes to the conclusion that if perforated gastric or duodenal ulcers are operated on within the first few hours after perforation, **resection** is the method of choice. If the conditions are favorable, this operation is to be preferred to suturing and especially to suturing in combination with a gastroenterostomy. It is also better than the operation in which a cuff of omentum is used. The patient's general condition is the decisive factor in determining the surgical method. If the patient is still in a good condition and if the perforation has not progressed too far, resection is the best method. The author employed it in 13 out of 29 cases. However, if the patient is already very weak, the quickest and safest method should be employed, either suture or the use of a **cuff of the omentum**. The author recommends a modification of the Billroth II method in combination with Braun's enteroanastomosis. He cautions that proper surgical care should be given to the duodenal stump. The advantages of this method are that the patient is

free from pain, that the conditions for the evacuation of the stomach are favorable, and that the tendency for development of a peptic jejunal ulcer is slight.

L. Grimault (Arch franco-belges de Chir 32 124 (Feb ) 1930) treated 10 cases of perforated ulcer by **excision** and **pyloroplasty**. The author states that this method is indicated in severe late conditions, when a rapid completion of the intervention is necessary, or if simple suture or burying of the perforation by a purse-string suture cannot be done. Grimault points to the importance of careful choice of the operative method and advises excision with pyloroplasty only if other methods appear unfavorable. The only difficulty in this operation may be encountered through the lack of mobility of the duodenum, which was noted in 2 patients. One of the greatest advantages of the method is that the operation is limited to a comparatively small area which prevents spreading of an infection. It is important to make an extensive resection so that the sutures can be laid in healthy tissue.

The *end-results* of operations for perforated peptic ulcers have been studied by K. Neller (Arch f klin Chir 161 244 (Aug 26) 1930). The total number of cases reviewed was 579. Of these, 374 patients, 64.4 per cent, were free from any discomfort. As to the effect of the type of operation on the result: 63 per cent of those on whom a *gastroenterostomy* was performed, in addition to closing the perforation by *suture*, made no complaint and 61 per cent of those without *gastroenterostomy* were symptom-free. Neller considers that *resection* of the ulcer is the best procedure so far as permanent results are concerned, but because of the sever-

ity of this operation it is indicated only rarely, *i e*, when it can be performed easily, when the condition of the patient is good, and if performed soon after the perforation has taken place. As a rule, or rather as a routine treatment, **closing the perforation** and performing a **posterior gastroenterostomy** gives the best results.

#### **SYPHILIS OF STOMACH.—**

**Diagnosis.**—Basing his report upon 93 cases of gastric syphilis, G B Eusterman (J A M A 96 173 (Jan. 17) 1931) states that this condition is not as rare as it was formerly considered to be. In China this condition is fairly common. In Russia the incidence would seem to be higher than in the rest of Europe.

The diagnosis of gastric syphilis is made difficult by its resemblance to carcinoma, but there are a number of diagnostic points. The average age of patients in the author's series was 36 years, with most of the cases within the second, third and fourth decades of life. Symptoms varied widely, with the location and extent of the lesion, and according to presence or absence of complications. Achlorhydria was the rule. The x-ray findings were those of circumscribed or diffuse involvement of the wall of the stomach, producing contraction and stiffening, and absence of visible peristalsis. The pylorus was usually not obstructed and was frequently gaping. In 70 per cent of the cases the lesion was in the pyloric antrum, in 22 per cent. the location of the lesion in the pars media produced an hour-glass defect; in the remaining 8 per cent. the involvement was diffuse. As a rule, the gastric lumen was symmetrically and concentrically encircled by the lesion.

It is obvious that many cases of gas-

tric syphilis will continue to be mistaken for carcinoma, which condition it closely simulates. However, the cardinal signs of malignancy, palpable mass, retention, nausea, anorexia, anemia, cachexia and hemorrhage, were infrequent in the author's cases of gastric syphilis, and this diagnosis must be considered whenever the patient's general condition is better than would be inferred from his gastric defect, as revealed by the x-ray examination.

It is especially important that whenever a patient is known to have syphilis, his gastric lesion be considered syphilitic until proven otherwise. This practice will prevent a certain number of unwarranted resections due to mistakes in diagnosis.

L T LeWald (J A M A 96 179 (Jan 17) 1931) reviews a number of cases of gastric syphilis selected from his series of approximately 50 cases. He finds the condition more frequent than has been supposed, and emphasizes the value of a therapeutic test (comparison of x-ray appearances before and after a course of antiluetic treatment). This author cites many cases in which the experienced roentgenologist made a correct diagnosis of gastric syphilis.

#### **CARCINOMA OF STOMACH.**

**—Diagnosis.**—How early do physicians diagnose cancer of the stomach in themselves? W C Alvarez (J A M A 97 77 (July 11) 1931) analyzes 41 consecutive case histories of patients all operated on at Mayo Clinic in 7 years. In 20, symptoms were of fairly short duration, with average of about 12 months. In 8, it was 5 months or less. One patient never, at any time, suffered with indigestion. Often it was hard to understand how a physician could have let himself go for so long a time with-

out an x-ray examination. Able clinicians were just as careless as general practitioners in the "backwoods." In some, final disaster occurred because the patient had always been bothered by chronic indigestion and hence failed to become alarmed when symptoms grew severe.

In 7 it is almost certain that the cause of the first symptoms of indigestion was an ulcer. In 5 more it may well have been an ulcer, and in 9 others the early symptoms of cancer were more or less characteristic of ulcer. In 4 the pre-operative diagnosis at the Clinic was ulcer, and in 4 others diagnosis of cancer was made only at operation. In still another case the patient had been operated on elsewhere for ulcer without the true nature being recognized. Altogether, the question of ulcer intruded itself into the diagnosis in half of the cases, and in many, the too-ready acceptance of ulcer by the patient and his advisers led to the final disaster. It seems obvious that the only hope for a cure of cancer of stomach is through **excision** when it looks and behaves like a benign ulcer. It would help much if every sudden disturbance of digestion in a middle-aged or elderly patient would be looked on with grave suspicion.

**Surgical Treatment.\***—According to H. Finsterer (Arch f klin Chir 159:30 (Apr 24) 1930), the operability of gastric carcinoma, in the complete absence of clinically demonstrable metastases, can be determined only by exploratory laparotomy, which he performs in every case under local anesthesia. If resection is possible (he does not consider either local or general contraindications), he performs it; hence, his high mortality of 65 per cent.

If the tumor is confined to the stomach, the *mortality* is low (211 resections with 13 deaths, 6.1 per cent); whereas when the tumor has extended into other organs (pancreas, liver, colon) resection, with simultaneous resection of the involved parts of these organs, gives a high mortality (129 resections with 53 deaths, 41 per cent). In the advanced cases of the disease the mortality is high (37.9 per cent), although the mortality among all cases of resection is only 19.4 per cent. Advanced age has little bearing on the immediate results of resection but has considerable bearing on the final results. In the case of patients aged 60, the mortality of simple gastric resection is 6.9 per cent, whereas that of complicated resections is 38.6 per cent. The best results are obtained when the operation is done under local anesthesia and the postoperative treatment looks toward the prevention of pulmonary complications.

The *end-results* are better in the aged than in the young. In the author's material, 40 per cent of those over 60, and only 22 per cent of those under 40, did not have a recurrence in the following 5-year period. Thirty-one per cent of the simple resections and 30.8 per cent of complicated resections remained free from recurrence for from 5 to 18 years. The end-results of the ulcer-carcinoma are not so good as are those of the primary gastric carcinoma. Of the former group, only 20.7 per cent, and of the latter 35.8 per cent, remained free from recurrence after the 5-year period. He urges that every callous ulcer of the stomach should be resected before it has become carcinomatous.

Finsterer (*loc cit*) is convinced that the results of resection for carcinoma

\* See also Results of Gastric Resection

of the stomach can be improved only if these patients come to operation much earlier than they do now, and this can be assured only by the closest co-operation between patient, internist and surgeon, as well as by greater efforts to educate the laity as to the importance of early recognition and early operation of this and every other type of cancer.

E S Judd and J M Marshall (Surg Gynec Obst 50 1008 (June) 1930) report a case of diffuse scirrhus carcinoma of the linitis plastica type, a typical "*leather bottle*" stomach without any evidence of intraabdominal extension or metastasis. Since no portion of the stomach was suitable for anastomosis, the duodenum was divided about 1 cm below the pylorus and the duodenal stump was closed. The stomach was then freed from its omental attachments throughout its entire length. By using the stomach as a tractor, about 4 cm of the lower end of the esophagus could be seen below the diaphragm. A Brunner right angle, rubber-covered clamp was placed on the esophagus as high as possible and the esophagus was then severed about 1 cm above the cardiac sphincter. The stomach was then free and was removed. The proximal loop of the jejunum was next brought up through an opening made in the transverse mesocolon, and its side was anastomosed to the distal end of the esophagus with the use of one continuous row of silk and one row of chromic catgut sutures. Convalescence was uneventful. The patient left the hospital on the twenty-second day in good general condition. At that time she was taking her feedings at 90-minute intervals, 2500 calories daily without discomfort. Forty days after the operation, the patient reported that she was feeling well, gaining in strength, and eating 4 meals

each day. Untoward symptoms have not appeared.

E Beresow (Zentralbl f Chir 58 266 (Jan 31) 1931) records 2 personal cases of **total resection** of the stomach. He states that Uhlhorn, in 1927, was able to collect 30 cases which had ended in recovery. In most of these the Billroth II operation had been performed. Beresow's patients were both operated on by the Billroth I method, under local anesthesia, for carcinoma of the stomach. The first was a man, aged 51, whose illness was of 10 months' duration, death ensued on the day after operation. The second patient was a man, aged 50, who had been ill for 5 months, his recovery was uneventful.

#### **SARCOMA OF STOMACH.—**

Two cases of lymphoblastic sarcoma of the stomach still cured 6½ years and 3 years and 10 months after **resection** of the stomach are reported by R Leriche and E Irmann (Lyon chir 26 534 (Aug-Sept) 1929).

At The Mayo Clinic, from January, 1908, to July, 1929, some 54 examples of sarcoma (53 operations) have been studied and are analyzed by D C Balfour and J C McCann (Surg Gynec Obst 50 948 (June) 1930). The average age at diagnosis was 43, with a predominance of males of 25.1 per cent. In only 4 was a family history of malignant disease elicited. The average duration of symptoms before operation was 18 months (dyspepsia, pain, tumor, bleeding, weakness and vomiting). Thirteen gave a history of gastrointestinal hemorrhage. Free acid was present in the content of 60 per cent. The majority of lesions were diagnosed as carcinoma before operation. The tumor could be removed surgically in 36 cases, while it was inoperable in 15. Treatment consisted, when possible, of par-



tial gastrectomy followed by Coley's toxins and x-rays in suitable cases. The tumors varied considerably in size, and several types were reported by the pathologist. Neither the type nor metastasis threw much light on prognosis. The immediate operative mortality for the whole group was 11.3 per cent. The postoperative duration of life in the cases in which only exploration was done averaged 4 months. The average life after operation of those patients who underwent resection and have died was 11 months. The average postoperative duration for the 12 living when last heard from has been 5 years, 1 has lived for 9 years.

**RESULTS OF GASTRIC RESECTION.**—Physiological and chemical studies following successful total gastrectomy for carcinoma have been observed by W. Walters (J. A. M. A. 95:102 (July 12) 1930). He states that the indications for and advisability of total gastrectomy for carcinoma of the stomach and the postoperative results present many interesting problems for investigation, among which are the effect of the loss of the acid and chloride normally secreted by the stomach and the explanation of the secondary anemia which has been reported as having occurred as long as 3 years after the operation.

At The Mayo Clinic, a gastrectomy is classified as a total gastrectomy only if no portion of the stomach is allowed to remain. The entire stomach has been removed for carcinoma 8 times at The Mayo Clinic. Four of the patients recovered from the operation. The patient on whom Walters operated has been well for more than 4 months. The operation was performed for an extensive scirrhus carcinoma of the linitis plastica type.

Studies of the *chemical changes* in the blood and of the cell count over a period of 4 months have revealed no appreciable change in the content of hemoglobin, the carbon-dioxide combining power, the concentration of blood chlorides or urea, or the number of erythrocytes. No evidence of a definite alkaline tide has been found. This is of interest, as it has been recognized that with the secretion of gastric juice in a normal person the urine tends to become more alkaline. The findings made in Walters' case, so far, appear to indicate that the lack of a stomach and its acid-secreting glands has a definite effect on the morning alkaline tide.

The absence of *secondary anemia* in experimental animals after total gastrectomy performed more than 4 years ago raises the question whether the cause of secondary anemia in human beings subjected to total gastrectomy is the result of local recurrence of the malignant growth or a remote metastasis. Brigham, Moynihan and Mayo have reported cases of great interest in this respect. In Brigham's case, in which the anastomosis was between the esophagus and the duodenum, the patient was well for 2 years following total gastrectomy and the normal formula of the blood was not affected. In Moynihan's case, that of a patient who lived 3 years and 8 months after the operation, marked anemia occurred, but no evidence of recurrence of the carcinoma was found at postmortem examination. In the case in which gastrectomy was performed successfully by W. J. Mayo, the patient lived for almost 4 years after the operation, but developed marked secondary anemia before death.

*Functioning of the stomach and pancreas* following extensive resection of the stomach has been studied by G. Stern

(Wien klin Wchnsch 42 557 (Dec 5) 1920), who reports the results of control examination in 107 patients who had been operated on for *ulcers* of the stomach according to Billroth's first or second method. In many cases the chemical tests revealed a marked decrease in pepsin and lab (ferment of rennet). Anacidity was found in nearly all patients, both in those that had been operated on according to Billroth's first method and in those in whom resection had been done according to Billroth's second method. From this the author concludes that the anacidity does not depend on the method of operation, but that it is the result of the extensive resection. It appears that by regurgitation of bile acids, trypsin digestion is activated in the stomach and compensates for the missing hydrochloric acid and pepsin. Neither the ferments of the pancreas nor the blood picture are affected by the resection. On the basis of his observations, the author concludes that the digestive apparatus is capable of adjusting itself to the changed conditions that result from resection. The general condition of the patients as well as control x-ray examinations proved that resection of the stomach gives satisfactory results in most cases.

I Danicico (Arch d. mal de l'app digestif 20 40 (Jan) 1930) observed that the nutritive balance in 19 cases of resection of the stomach showed a deficiency in the utilization of fat and an insufficiency in the utilization of proteins. The deficiency in the utilization of fat is proved by the lowering of the coefficient of absorption of all fats. In the 19 cases the minimum value was 74 per cent and the average was 88 per cent. The function of the remaining portion of the stomach, after resection, has a certain rôle in determining the

utilization of fats. The gastric deficit is compensated for by greater intestinal digestive activity.

## STOMACH, RUPTURE OF. See ABDOMINAL INJURIES

**STRABISMUS.—ETIOLOGY.**—R K Lambert and C E McDannald (Am J Ophth 14 46 (Jan) 1931) report high hyperopia and convergent strabismus in a mother and 4 of her 7 children. Nystagmus occurred in 3 and optic pseudoneuritis in 4 of the patients. There was no history of consanguinity.

Convergent strabismus is attributed by P A Harry (Prescriber (Nov) 1929) to a neuropathic tendency inherited by children from their parents. He does not attach much importance to the numerous other theories which include muscular malformations, refractive errors, and defective fusion sense. He believes, however, that the theory of excessive innervation explains the etiology of the defect in children between 2 and 4 years. He allows 6 months' experimentation with the necessary **correction**, attempting to reestablish central fixation and to restore binocular vision. If this fails, **operation** is advisable to prevent amblyopia, muscular changes and the loss of desire for binocular vision.

Squint is considered by O Barkan, H Barkan, H O Randel and H G Smith (Arch Ophth 5 691 (May) 1931) to be due to an inherited general nervous instability. They advise the **cinch shortening operation** (O'Connor's operation) and **correction** of strabismus at an **early age**, before structural muscle changes and amblyopia have developed, and while the fusion faculty can still be developed.

**TREATMENT.**—F N Knapp (Minnesota Med 14 324 (Apr) 1931)

considers that operative procedures for the relief of strabismus should be performed before school age in order to prevent amblyopia ex anopsia. Strabismus is not outgrown.

Good results were obtained by S. R. Gifford (*Arch. Ophth.* 2: 651 (Dec.) 1929) in 3 cases of paralytic strabismus by **muscle transplantation** of part of the active recti to replace the paralyzed muscle. He performs complete tenotomy of the opposing muscle and exposes the paretic muscle and 2 recti muscles. The outer third of each active rectus is then freed from its insertion and sutured through and beneath the tendon of the paretic muscle. Sutures are removed on the tenth day.

A method of performing **tenotomy** is described by M. Goldenburg (*Am. J. Ophth.* 14: 648 (July) 1931). In order to avoid the uncertainty of its reinsertion, the tenotomized muscle is controlled by suturing it to the conjunctiva.

W. B. Lancaster (*Ibid.* 14: 483 (June) 1931) claims more certainty, accuracy, and ease of performance, by his **muscle shortening operation** with buried sutures.

As a routine treatment of convergent squint due to errors of refraction, M. E. Smukler (*Ibid.* 14: 808 (Aug.) 1931) recommends stretching the opponent muscle and **tucking** of the external recti muscles. He finds this the most effective procedure when the squint exceeds 15 degrees in children past the age of 12, in whom nonoperative means have failed. He describes a special tucking instrument and curette for use in this method.

The **tucking operation** is recommended by F. E. Burch and H. W. Grant (*Ibid.* 14: 489 (June) 1931) for its safety and ease of performance. They point out that cyclophoria or ver-

tical deviation is avoided by preservation of the original insertion and that the correction obtained is more permanent than by any other method. After the second week the disagreeable prominence is rarely noticed. Tucking should usually be combined with recession.

**SUPRARENAL GLANDS.** See ADRENAL GLANDS, also ANIMAL EXTRACTS. ADRENAL ORGANO THERAPY.

**SYPHILIS.—INCIDENCE.**—The incidence of syphilis in general practice has been studied by Eli Grimes (*J. Iowa M. Soc.* 21: 108 (Mar.) 1931), who reports that in 15,000 individuals, a positive diagnosis was made in 674 cases, or 4½ per cent. When it is taken into consideration that syphilis has a long period of latency during which it is beyond recognition, it is reasonable to conclude that the incidence is much higher. Six per cent would be a conservative estimate. The extent of the problem of syphilis in the United States has been estimated by T. Parran, Jr., and L. J. Usilton (*Am. J. Syph.* 14: 145 (Apr.) 1930) on case rates of 4.77 for males and 3.08 for females to be 643,000 cases. The peak age group was found to be from 20 to 25 years.

A recent study of the rural negro in a Southern state indicated that as high as 24 per cent of the entire population of more than 1 year of age showed a positive Wassermann reaction. The results of a number of published reports over a 10-year period indicate that of women admitted to maternity hospitals, 6.9 per cent had a positive Wassermann reaction. Dementia paralytica contributes 4 per cent of the population of institutions for mental disorders. The attack rate for syphilis, as determined by a study of the new cases admitted to treatment during a 1-month period in a city

of the United States with a population of 2,000,000 inhabitants, is represented by 3.46. Syphilis stands first or second among the most frequently reported infections to the Public Health Service from the several state health departments.

**Race and Sex Distribution.**—In a total of 10,000 ambulatory patients above the age of 12 years known to have syphilis, whose histories were reviewed by T. B. Turner (Bull. Johns Hopkins Hosp. 46:159 (Feb.) 1930), the total number of cases was approximately equally divided among the 3 stages of syphilis, *i. e.*, early, tertiary and latent. Of the total patients, 3.4 per cent had congenital syphilis. During the past 10 years a steady decline has been noted in the number of cases of early syphilis, *i. e.*, of recent infections, in white persons, especially white males. Genital chancres were rarely observed in females.

Reinfection was found to be more than 7 times as frequent in males as in females. Acute iritis occurred in 5.5 per cent of patients with secondary syphilis, although it was twice as frequent in negroes as in white persons. The incidence of acute meningitis in the white race was approximately twice that in negroes, and in males twice that in females. The incidence of neurorecurrence was higher in whites than in negroes, and higher in males than in females. Lesions of the skin and mucous membranes occurred with about equal frequency in both races and both sexes. The incidence in the total late cases was 8.8 per cent. Lesions of the skeletal system were observed in 8.8 per cent. of the total late cases. Syphilitic stricture of the rectum was confined almost entirely to colored females. Gumma of the lymph nodes was an un-

common manifestation. It occurred preponderantly in negroes.

Clinically recognizable syphilitic involvement of the cardiovascular system, exclusive of cerebral vascular lesions, occurred in 10 per cent of all late cases, the proportion of males to females and of negroes to whites was approximately 2 to 1. Uncomplicated aortitis, with or without aneurism, occurred much more frequently in males than in females and in negroes than in whites. Aortic regurgitation was more than twice as common in males as in females, although it was nearly as common in white as in negroes. Syphilitic angina pectoris was rare but was more common in whites and in males, respectively, than in negroes and females.

Central nervous system syphilis was observed in late syphilis in 39.3 per cent of white males, in 22.3 per cent of white females, in 15.9 per cent. of colored males, and in 7.0 per cent of colored females. Dementia paralytica was 7 times as frequent in white persons as in negroes, and 28 times as frequent in white men as in colored women. Tabes dorsalis, with or without optic atrophy or Charcot joint, was much more common in white males than in white females or in negroes of either sex. It was exceedingly rare in negro females. Cerebral vascular syphilis was observed somewhat more frequently in negroes than in whites.

**ETIOLOGY.**—In discussing the virulence of *Spirochæta pallida* in culture, J. A. Gammel and E. E. Ecker (Arch. Dermat. and Syph. 23:439 (Mar.) 1931) state that 72 hours following the removal of syphilitic tissues from the host, spirochetes which may be morphologically typical and motile failed to infect rabbits when inoculated intratesticularly. Similarly, in certain me-

diums (gelatinized human, sheep and rabbit serums) typical and motile spirochetes were observed for a period of weeks and months, but they failed to grow in subcultures. These cultures, also, even if they retained their morphologic characteristics and motility, did not retain their virulence for rabbits for more than 48 hours. There is no parallelism between motility and virulence. At present, no reliable culture medium is known in which virulent spirochetes can be successfully grown.

**Life Cycle of Syphilitic Virus.**—

Lépine (Presse méd 39 1233 (Aug 19) 1931) summarizes the theories of the etiology of syphilis. Lavaditi and Lépine proved that positive reactions, as demonstrated by Wassermann and Meinicke tests, are independent of the virulence of the organism, state of the infection or immunity of the host. They proved this by animal inoculations with heat killed spirochetes. According to recent work, *Spirochæta pallida* in itself is not the causative agent, but, instead, a visible and nonvirulent stage in the life cycle of an ultravirus and virulent stage. Observation of human patients and many experimental animals lead the author to the following conclusions. Many syphilitic conditions do not harbor the visible spirochete. Animal experiments prove that in the life cycle of the spirochete there is present a first stage, in which only the virulent invisible agent exists; a second stage, in which there are present both spirochetes and the virulent invisible agents; and the third stage, containing a nonvirulent vegetative form resembling the recurrent spirochete or the spirochete of parasyphilis. The invisible agent is an ultravirus.

***Spirochæta Pallida.***—M. D. Yushkov and K. P. Astvazaturov (Vrach

Gaz 7 510 (Apr 15) 1931) undertook the study of 500 observations in regard to the influence on *Spirochæta pallida* of various substances, as (1) agents used in the prophylaxis and therapy of syphilis, (2) some physiologic substances of the human body, and (3) of some nutritive materials in wide use (as a factor in the nonsexual spread of syphilis). The authors conclude that (1) it must be assumed that *Spirochæta pallida*, with considerable deformation under the action of some injurious agents, undoubtedly loses its syphilitic virus, whereas its avirulence with the loss of motility and with slight morphologic substances of the human body, and experimental infection. (2) The most certain prophylactic antisiphilitic agents are fresh solutions of corrosive mercuric chloride (1:1000 and 1:2000), solutions of phenol (from 1 to 2 per cent), denatured alcohol, ethyl alcohol and the foam of *sapo viridis*. (3) The foams of *sapo domesticus* and all dilute aqueous alcoholic solutions do not possess enough disinfectant power. (4) Among the eye remedies, the best as a prophylactic measure is a 0.5 per cent solution of silver nitrate, which has strong coagulating power. (5) Solutions of arsphenamine and of iodine salts do not have *in vitro* a spirocheticidal action. (6) *Spirochæta pallida* demonstrates an increased sensibility toward acid and is more resistant to alkaline mediums. This can be explained by its biochemical properties and by the habitual environments that it encounters in the weakly alkaline reaction of the fluids of the human body. (7) The acidity of gastric juice, the strongly acid vaginal secretion and urine acidity stop the motility of the spirochetes, while blood serum, neutral saliva, slightly acid or alkaline urine do not. (8) Beer,

buttermilk, strong tea and various fruit juices also stop their motility, port wine, lemonade and other similar beverages with a high content of acid coagulate and dissolve them (9) Russian brandy does not stop their motility at once In fresh milk, as well as in brew mash and in running water, *Spirochæta pallida* conserves its normal motility

**Superinfection in Syphilis.**—O Thomsen (Hospitalstid ; Venereal Disease Information (Jan 20) 1930) believes, with Neissen, that superinfection can be produced in the period between the first inoculation or spontaneous infection until the chancre develops This susceptibility is continued in man until the appearance of the secondary rash Allergy of the infected system then prevents successful reinoculation The author believes that this conception of generalized infection draws a definite border line which is unwarranted These reactions are due to generalized infection and not to infection proper According to the author's opinion, the positive Wassermann reaction cannot be attributed to the later occurring non-susceptibility, which must be looked upon as other likewise effective immune processes

It is also the author's opinion that rabbit experiments alone cannot disprove the belief that superinfection with characteristic skin processes is produced in the virus Many reinfections have been reported Slight glandular swelling, rash, and abortive chancres, may appear, but these may also be so uncharacteristic that it is doubtful whether they are the results of the first infection. Quite often, however, the first infection is less marked as to symptoms than the reinfection Of late there has been a tendency to doubt the immunity of treated syphilis and an in-

clination to blame insufficient treatment for recurrence of symptoms In recent years, latency lasting for many years and with a positive Wassermann reaction has been considered rare It would be well to bear in mind also that in more advanced age new infections are rare These observations have generally been confirmed by animal experiments

**EXPERIMENTAL SYPHILIS.**—When rabbits were inoculated with syphilitic virus by A M Chesney and T B Turner (Bull Johns Hopkins Hosp 48 90 (Feb) 1931) in such a manner as to produce a lesion involving the skin, whether the original inoculation was made subcutaneously, intracutaneously or by depositing the virus on the surface of a granulating wound, subsequent inoculation with homologous virus after a period of 4 months or more was not followed by the development of lesions, no matter whether the second inoculation was made intratesticularly, subcutaneously, intracutaneously or intravenously. Intravenous reinoculation under these conditions may be followed by reinfection without lesions When syphilis develops in rabbits after intratesticular inoculation, a second inoculation with homologous virus by the intracutaneous route after a period of 4 months or more is not followed by the development of any lesions at the site of inoculation When syphilitic virus is injected intravenously into rabbits, marked and widespread lesions of the skin and bones develop When these animals are reinoculated with homologous virus after a period of several months, whether by subcutaneous or intracutaneous injections, no lesions develop However, intravenous injections under these circumstances may be followed by reinfection but without lesions



T. Tam, M. Kakishita, and K. Saito (Zentralbl f. Bakteriol. (Abt. 1) 117: 73 (June 3) 1930) find that guinea-pigs inoculated intratesticularly with suspensions of syphilitic rabbit's testicle do not contract syphilis. If, however, the inoculation is made intracutaneously into the scrotum, about 55 per cent of the animals show chancres. The inoculation period may last from 1 to 6 weeks, but is generally about 17 days, and the lesions persist, as a rule, for about a fortnight. It was observed that in these rabbits swellings sometimes developed in the perineal fold; examination of the fluid obtained from them by scarification revealed the presence of spirochetes morphologically indistinguishable from *Trep. pallidum*. Experiments were, therefore, made to determine whether primary inoculation into the perineal fold would result in the development of syphilis. It was found that inoculation of syphilitic rabbit's testicle uniformly gave rise to lesions in this situation. The inoculation was made intracutaneously into the inner raw part of the perineal fold which appears when the scrotal sac is drawn outwards with the fingers. After an incubation period of about 11 days a swelling appeared, this spread over the whole inner surface of the inoculated side and, later on, to the opposite side. It lasted, as a rule, for about 7 weeks. By scarifying the lesion and inoculating the juice into the perineal fold of a fresh guinea-pig, it was possible to reproduce the disease in at least 6 successive animals. Inoculation by this route with rabbit material was uniformly successful, and it would, therefore, appear to be more satisfactory than scrotal inoculation. This route was likewise found to be suitable for the direct inoculation of human syphilitic material.

The lymph-gland transfer method for determination of the presence of the *Trep. pallidum* in human cases of syphilis was applied in 66 instances by G. C. Lake and K. K. Bryant (Nat. Inst. Health Bull. No. 157). The group includes 34 early untreated cases, 15 early partially treated cases, 9 insufficiently treated old cases (average duration 6.9 years), and 8 untreated old cases (average duration 22.5 years). They were able to demonstrate the spirochete in the testicles of rabbits inoculated with emulsified lymph glands from each of the 34 early treated cases and from 4 of the 9 insufficiently treated old cases. All of the other transfers proved negative, even after subculture to a second group of animals. The results which they obtained indicate the impracticability of using the intratesticular injection of human lymph-gland emulsions into rabbits as a method for determining the presence or absence of syphilis in man, except in the early untreated stages. Similarly, their work shows the impracticability of applying this method to the measurement of the chemotherapeutic activity of the arsenicals in the treatment of syphilis in man.

The results which Lake and Bryant obtained in the production of syphilis in the rabbit indicate that if careful clinical examinations are frequently made of the original group of inoculated animals, if sensitive and dependable serological tests are employed, and if final dark-field examinations are made of an emulsion of the entire inoculated testicle from these rabbits, subsequent subculturing of the negative animals into a second group of rabbits will not significantly increase the number of positive findings. The additional time and expense involved outweighed the results to be expected.

*Tissue transplants in the diagnosis of the cure of syphilis* with especial reference to lymph nodes, skin and leukoplakia have been studied by S S Greenbaum (J A M A 94 1464 (May 10) 1930) In the 23 glands studied it was found that those from patients with untreated acute early syphilis always contained *Spirochæta pallida*, but that this was true in only about 43 per cent of patients with untreated chronic syphilis Of 16 skin transplants from patients in all stages of syphilis, 2 gave positive results Transplants from 2 leukoplaques gave negative results Human gland transplants cannot be used as a means of determining cure in syphilis since *Spirochæta pallida* disappear from these glands spontaneously in many untreated and uncured cases. If they are not invariably present in untreated cases, their absence in treated cases would be of no value so far as a criterion of cure is concerned The disappearance of the secondary rash of syphilis does not always mean destruction *in situ* of all spirochetes causing that rash The finding of residual spirochetes in 2 instances out of 16 skin transplants studied suggests the reason for the development of gummas in later life. In other words, the fact accepted as fundamental, *i.e.*, that all spirochetes in early lesions are slowly destroyed, is not always true In some instances their pathogenic action is merely repressed and they are not completely eliminated. Persistently enlarged glands in patients with syphilis are no indication of the presence or absence of *Spirochæta pallida* in such glands

**PATHOGENESIS.**—In a study of *reinfection* in syphilis, J. H. Stokes, A G Schoch and F A Ireland (Arch Dermat and Syph 23 829 (May) 1931) present the results of a survey

of 2439 cases of syphilis, 913 of which were in the primary and secondary stages Among these cases there appeared 56 early mucocutaneous relapses and 4 possible second infections These observers state that reinfection, while a conspicuous element in the literature, is only one-fourteenth as common as relapse and one-sixty-seventh as common as first infection with syphilis The weaknesses of existing material on reinfection with respect to historical detail, adenopathy, the scar and site of the chancre, examination of the spinal fluid and adequate physical examination, are briefly summarized.

Reported reinfections and their own 4 cases are classified by Stokes and his co-workers on 3 grades of strictness of criteria, with categories of indisputable, probable, and possible reinfection, which are defined Thus reclassified, it appears that there are no indisputable reinfections, the evidence for which conforms to every requirement; about 116 conform to a moderately rigid standard and 120 conform to an average standard, which, in their opinion, is too lax to provide for confusion elements of morphology It is suggested that the highest ideal of syphilologic reporting would be the presentation of cases of "airtight" reinfection, if such a thing exists. Between enthusiasm, subjectivity and unpreparedness for the usually unexpected appearance of these cases, the large majority of reports are useless, and in the authors' opinion, no irrefragible clinical entity of second infection with syphilis has been established.

In a summary of the facts of *infectiousness* in syphilis, J H. Stokes (J M Soc New Jersey 28:391 (May) 1931) asserts that the more recent the infection, the more dangerous. The

blood Wassermann reaction is not a guide to infectiousness or noninfectiousness. It may be negative with infectious lesions present, and positive in noninfectious cases. The most infectious lesions are chancre, mucous patch, condyloma and moist papule (flexures). The places to look for infectious recurrent lesions in inspection are the lip (outer and inner surfaces), angles of the mouth, faucial pillars and tonsils, sides and bottom of the tongue, the axilla, nipples, inguinal folds, labia, penis, scrotum, and anus (hemorrhoids). All open or eroded lesions in early syphilis are dangerous. Infection is also transmitted by semen and by benign nonsyphilitic lesions (herpes) in patients with syphilis. Syphilis is transmitted mainly by intimate contact with moist surfaces, *i e*, by kissing or sexual intercourse. Moist articles and discharge-bearing dressings, as well as articles of common use, can also carry infection. Thorough washing in hot water and soap will disinfect contaminated objects. The additional precaution may be taken of boiling dishes, utensils and such articles as douche nozzles and instruments in solution of sodium bicarbonate. Dry objects and dry (not crusted) lesions are noninfectious. Pyogenic infection reduces the infectiousness of the local lesion. Trauma by an infected object (the knuckle striking the teeth, a needle prick) makes infection almost certain, it may be hematogenous and without chancre. Transfusion is also a means of transmitting syphilis. A single negative blood Wassermann test in the donor does not afford protection.

There is a distinct *infectious relapsing type* of syphilis that must be watched for. To a patient with this type of syphilis, no assurance can be made. Local irri-

tation, such as is caused by dirt, sweat, discharges, friction (intercourse), and tobacco (smoked or chewed), favors infectious recurrence. Time diminishes the infectiousness of syphilis. After 5 years, few patients are infectious, desultory, noncurative treatment, with relapses, may prolong infectiousness many months or years. No treatment can guarantee the noninfectiousness of syphilis indefinitely. Secondary relapses have been seen with dementia paralytica after 20 years. Inadequate treatment favors infectious relapse. Late syphilids are not infectious, even though open lesions are present. They should not be confused with recurrences. Mercury does not control infectiousness. Bismuth, while more effective than mercury in this respect, is probably less so than arsphenamine, the latter being able to control infectiousness probably as long as 1 month from the last dose.

The attention of the medical profession is called by S. H. Polayes and M. Lederer (*Am J Syph* 15:72 (Jan) 1931) to the possibility of transmitting syphilis from donor to recipient or *vice versa* in the performance of *blood transfusions*. Ten cases of this nature reported in the literature since 1917 are reviewed, and an additional case of an infant developing syphilis following a blood transfusion is described by the authors. Difficulties are encountered in determining whether or not the blood of a given donor is infectious. Cases are cited to prove that neither the absence of clinical signs, nor a negative blood Wassermann reaction entirely excludes the possibility of the existence of syphilis in the donor. It is urged that family donors should submit to the same rigid physical and serological examination as professional donors because, in a large percentage of the cases, family

donors were responsible for the transmission of syphilis to the recipients

A case of syphilis developing after *blood transfusion* is reported by C Aubertin and J Fleury (Bull et mém Soc méd d hôp de Paris 54 69 (Jan 27) 1930) The patient had received 5 transfusions, 15 days apart, for extreme anemia The eruption occurred about 65 days after the first transfusion About 5 days before the appearance of the eruption and exactly 2 months after the first transfusion, the Wassermann reaction had been negative Other sources of infection were ruled out

**PATHOLOGY**—A study of 1675 autopsies on individuals over 25 years of age in the years 1909 to 1929 has been made by Aldred Scott Warthin (Proc Inst Med Chicago 8·173 (Feb 15) 1931) Of this number, 408 males and 86 females showed tissue lesions that in the author's opinion represent active latent lesions of syphilis

Among the practical conclusions to be drawn from this study is the great importance of latent syphilis either primarily or secondarily leading to the production of cardiovascular disease Myocardial insufficiency was the chief cause of death in his material Warthin made a detailed study of the occurrence of coronary sclerosis, coronary thrombosis, angina pectoris, myocardial infarction, and sudden death, in both his syphilitic and nonsyphilitic autopsies Syphilis of the larger coronary branches has been rare in the editor's experience, and he had only 2 cases of angina pectoris associated with an active coronary syphilitic arteritis and thrombosis Myocardial syphilis is essentially a disease of the smallest coronary branches, the intermuscular capillaries and small arterioles being especially involved Nevertheless, syphilis is an indirect etiological

factor in the production of coronary sclerosis and angina pectoris, since these latter conditions are more than 5 times as frequent in his cases showing lesions of latent syphilis, as in those presenting no such lesions The same thing is true of myocardial infarction, fibrosis due to a healed interstitial myocarditis, presumably syphilitic, and of sudden cardiac death Syphilis is undoubtedly a secondary factor of great importance in the etiology of sclerosis A very large proportion of the cases of aortic sclerosis that show no gross characteristics of syphilitic aortitis, are found on microscopic examination to be due to syphilitic obliteration of the arterioles of the vasa vasorum, thus producing a slow infarction or sclerosis of the intima It must be emphasized that his diagnoses of syphilis were based wholly upon microscopical criteria The tissue lesions described and interpreted as syphilitic in nature have been over and over again found associated with typical spirochetes of the pallida form, so that the author regards them as pathognomonic, even in the absence of the latter

From his histologic examinations of various syphilitic changes, J Almquist (Hygiea 93 481 (July 15) 1931) concludes that there are unlike characteristic changes in each of the different tissues, that these changes are in the main the same both in older and more recent stages of syphilis and allow no division into 3 periods, and that the different appearance of the various clinical syphilitic changes depends on the localization of *Spirochæta pallida* in the tissues, also on variations in immunity, action of toxins and antitoxins, nutritive disturbances and other factors He describes infiltrative and late degenerative changes and epithelial and endothelial proliferation, together with pustular and necrotic

changes, and differentiates cutaneous syphilitic changes into 6 types. His incomplete investigations on syphilis of the inner organs and the nervous system point to changes, with the absence of pustule formation.

In histologically typical lesions of syphilis, A. S. Warthin and R. E. Olsen (Am J Syph 15:145 (Apr) 1931) demonstrates by specific staining methods certain intracellular forms which, because of their obvious connection to typical spirochetes, may be regarded as representing phases of the syphilitic organism. Of these forms, they describe the polymorphous or ring form, which may be connected to the typical spirochete, or more often to the fine spiral form, the lymphocytic granular form with intermediate spirochetal stages, and the fine threads and granules found in the giant cells. The intracellular polymorphous form and attached small spirochetes are widespread in their distribution and apparently are found in all syphilitic lesions, being least common in areas undergoing resolution. They may occur independently of the typical large spirochete form. Their staining reaction is such that they are not usually demonstrable by the standard spirochete staining methods.

The lymphocyte cell granular type is commonly found in lymphoid tissue during the early stage of syphilis and is usually absent in the later stages. The giant cell reaction forms are limited to the areas of resolution and occur only occasionally in the giant cells found in the late stages or in gummas. From the morphologic evidence it would appear that intracellular stages of *Spirochæta pallida* are being dealt with here. Their relations to the typical form appear so obvious and certain, and the assumption that these intracellular forms are asso-

ciated with *Spirochæta pallida* clears up so many of the problems attending the demonstration of the typical spirochete in syphilitic lesions, that the temptation is great to draw such conclusions.

But a conservative position must be taken in regard to this question, for however obvious the morphologic evidence may appear, still it can never be absolutely conclusive as to the positive nature of the relationship of apparently closely related forms. The ultimate settlement of this question must rest on experimental evidence.

In a case of fatal malignant syphilis reported by U. J. Wile, L. Wieder and A. S. Warthin (Am J Syph 14:1 (Jan) 1930) occurring in a man 24 years of age, who presented 325 distinct ulcerative skin lesions and a maculopapular eruption, the ulcerative lesions were found on microscopic study to be sharply circumscribed anemic infections of the corium and epidermis, due to thrombosis of the cutaneous vessels secondary to syphilitic obliteration of medium-sized vessels at the borders of the corium and subcutaneous tissues. The great size, sharp borders, scanty exudate, and cone-shaped form of the ulcers, the absence of histological lesions of syphilis in their borders, and the absence of spirochetes in the lesions were explained by the secondary infarction process. The malignancy of the syphilitic process was evidenced by the almost complete involvement of the dermal vessels which led to obliteration of these vessels, thrombosis, and consequent infarction of large areas of the skin.

This is a new explanation of the cutaneous lesions of malignant syphilis. No case like it has been described in the literature. Whether the pathological findings will explain other cases ap-

pearing clinically as malignant syphilis, or whether this case was unique, remains to be determined from the study of other cases presenting a similar clinical appearance. If other cases should be found to exhibit the same picture of vascular syphilis, obliteration of vessels, secondary thrombosis, and infarction, more light will be thrown on the nature of the most severe forms of dermal syphilis. In the authors' case there was an undoubted susceptibility to the spirochetes on the part of the small blood-vessels in various regions of the body. The patient was particularly resistant to treatment, but this was in part only apparent, since most of the seemingly syphilitic lesions of the skin were not directly syphilitic but were necrotic lesions of a secondary infarction. That the treatment was effective so far as the spirochetes were concerned, was shown by the enormous number of degenerating organisms found in the tissues. Just when this great destruction of spirochetes took place, it is impossible to say.

The case was unique also in the extensive visceral involvement (thyroid, heart, pancreas, and urinary bladder). It must be remembered, however, that few autopsies and fewer microscopic studies have been made in cases of malignant syphilis.

The evidence suggested that the syphilis was acquired. If this is correct, the patient was the youngest patient with acquired syphilitic myocarditis on record.

Microscopic study of the heart showed a small amount of subepicardial fat with serous atrophy. Beneath the endocardium the muscle presented marked fatty degenerative infiltration. Throughout the myocardium there were numerous diffuse lymphocyte and plasma-cell

infiltrations arranged around the smallest coronary arteries. Many areas showed the intermuscular single-file arrangement of nuclei characteristic of syphilitic myocarditis. In other areas the cellular infiltrations were grouped into larger masses suggesting miliary gummata. Beneath the endocardium there were localized areas of cellular infiltration. In places, this infiltration produced a thickening of the endocardium itself. There was no involvement of the larger coronary branches.

Syphilitic juxtaarticular nodes occurring in 3 men who had never been in the tropics are described clinically and histologically by L. A. Brunsting (Am J Syph 15:42 (Jan) 1931). Definite evidence of syphilis was present in each case, and the Wassermann reaction was uniformly positive.

It is pointed out by P. Neuda (Wien Arch f. inn. Med 21:455 (July 15) 1931) that the clinical analysis of the iodine tolerance of syphilitic patients indicates qualitative changes of the body lipoids. The chemical analysis of the *blood lipoids* in normal persons and in syphilitic patients corroborates this assumption. It could be demonstrated that the phosphatides showed an absolute and relative increase in comparison to the total lipid content, and in some of the cases the total lipid content was likewise increased. The determination of the iodine number in syphilitic patients revealed an increase of unsaturated fatty acids. It is assumed that the 2 conditions have a certain relationship in that the qualitative changes of the blood lipoids create a predisposition for the development of unsaturated fatty acids.

H. C. Gjessing (Norsk mag f. laegevidensk 91 716 (July) 1930) records 9 cases of *jaundice* which oc-



occurred among the male syphilitic patients at the Ullevål Hospital in the period 1922-30, it appeared in 3 at the beginning of treatment by salvarsan, in 4 during its course, and in 2 after the treatment had ended. He maintains that most of the cases of jaundice occurring in the course of salvarsan treatment are of an infective nature, because an increased frequency of jaundice among syphilitic patients is accompanied by a rise in the incidence of jaundice in the rest of the population. In some cases, however, it may be difficult to determine the cause of the jaundice. In the author's 3 cases in which it occurred at the beginning of treatment, the jaundice was regarded as syphilitic, principally because it was associated with other syphilitic symptoms, and was therefore treated with neosalvarsan. The disappearance of jaundice, however, under treatment by salvarsan is no proof that the jaundice is syphilitic, since it may disappear without specific treatment, and there is always the possibility that a number of microorganisms which produce jaundice, besides that of syphilis, are affected by salvarsan. Although the author has treated cases of jaundice in syphilis by arsenobenzol preparations without complications, he considers it advisable, in view of the fatal cases on record, to stop the specific treatment on the appearance of jaundice, and to resume it only when the jaundice has disappeared.

K. Zieler (*Deutsche med. Wchnschr.* 57. 393 (Mar. 6) 1931) studied to what extent the *function of the liver* is influenced by syphilis or by syphilis therapy. Ninety-seven syphilitic patients undergoing arsphenamine, bismuth or mercury treatments were subjected to various tests before, during and after the treatment. The tests were of 4 types

(1) examination of the hepatic function without any intervention, such as determination of the urobilinogen in the urine and of the bilirubin in the blood, (2) bilirubin tolerance test, (3) tolerance tests with foreign substances such as tetrachlorophenolphthalein, and (4) Volhard's water tolerance test.

The regular control of the liver function in the course of syphilis therapy has proved that the intensive treatment with arsphenamine and bismuth or with mercury, as it is now practiced, rarely causes functional disturbances of the liver, and if it does, the disorders are only slight and of short duration. In rare cases, complications may arise from a hypersusceptibility to the medicaments. The slight hepatic disturbances that develop in the course of syphilis therapy are much less severe than those hepatic disorders that develop if syphilis is not treated.

It was noted in cases in which syphilis was complicated with other diseases, such as gonorrhea, and in instances in which malaria therapy or specific treatment of gonorrhea became necessary, disturbances of the liver were more frequent. These disturbances became manifest in the positive reactions of one or several of the functional tests. Positive reactions of several tests is a grave sign, even if there are no clinical signs of an hepatic disturbance. The author comes to the conclusion that the control of the liver function in the course of the syphilis therapy is of great significance and should be done in all hospitals. In evaluating the various tests, he states that the determination of the urobilinogen in the urine is the most significant and, because the test is at the same time extremely simple, it can be performed by the general practitioner.

**SYMPTOMATOLOGY.—*Pseudotuberculous Forms of Tertiary Syphilis of the Nose and Pharynx.***

—Of all the manifestations of tertiary or delayed congenital syphilis, the most common, according to A. Aubin and R. Maduro (Arch. internat. de laryng. 9: 805 (July-Aug.) 1930) are lesions of the nose and pharynx. In observing numerous cases, the authors have been impressed by the considerable percentage of nasal lesions which present an aspect quite different from the standard descriptions. Usually the lesions in the nose are not diffuse infiltrations or gummata, but resemble very closely lupus of the mucous membranes. In the pharynx, on the contrary, the gummatous form of lesion is the most common. However, even this often resembles tuberculous granuloma of the milium type (Isambert's disease).

The classical luetic lesions of the nose are characterized by swelling, obstruction and pain. At first they are dry, but with breaking down of the granuloma, a foul discharge appears. This is coincident with the formation of sequestra. The initial stage of the disease is seldom seen. Once developed, the gumma or diffuse infiltration located on the septum resembles a hematoma. It never involves the cartilage. Lesions on the inferior turbinate suggest a simple hypertrophy. According to the classical descriptions, the broken-down lesions resemble a punched-out ulcer, but in reality this aspect is almost never seen. The common lesion is the lupoid form, resembling tuberculosis in appearance, but is less torpid in its course. The lesion presents granulations and an irregular mulberry-like surface which bleeds easily. The base of the ulcer is indurated and often shows the underlying bone (Lubet-Barbon).

The lupoid form of tertiary syphilis little suggests the disease. There is no pain, no swelling of the nose, and little obstruction. The patient suffers simply from slight but constant difficulty in breathing, an ordinary mucopurulent discharge, and sometimes thin crusts, the removal of which causes slight bleeding. Examination reveals one or more ulcers with ill-defined and irregular borders and a base covered with granulations the size of a pin-head. Often the cartilaginous septum is involved, but there is no exposure of cartilage or bone. This is the description of lupus, but a difference is seen in the infiltration of the surrounding mucosa which is definitely red.

In the pharynx, in which gummatous and ulcerative types of syphilitic lesions are most common, the early stage of infiltration is seldom observed. Usually the patient presents himself with an ulcer of the classical type, which shows a yellowish base and punched-out scalloped borders and is surrounded by intensely hyperemic mucosa. Pain is absent. As a rule, there is only a single lesion, but it is large, and in healing it leaves white contractile cicatrices.

In the pharynx, the pseudolupus form is rare, but may very closely simulate lupus. The pseudotuberculous form of pharyngeal syphilis appears under the guise of *Isambert's disease* (milium tuberculosis of the mucosa). Multiple ulcers develop in successive crops as the result of the softening of milium gummata. The latter present themselves as minute yellow bodies the size of sago grains, which are surrounded by a bright red zone of infiltration. The ulcers become confluent and cause extensive losses of substance. New milium gummata constantly appear in the vicinity. It is on the posterior wall of

the pharynx, the soft palate, and the nasal mucosa that syphilis reproduces most exactly the tuberculous granuloma of Isambert. While the presence of fever and the absence of surrounding zones of infiltration are supposed to distinguish tuberculosis from syphilis, the differences are often more theoretical than real.

Because the clinical symptoms of these special forms of syphilis are insufficient to differentiate them from tuberculosis, the authors discuss the various elements in the diagnosis in detail.

*Diagnosis* by means of *biopsy* is very delicate. In syphilis, the lesions are well vascularized, the intima of the vessels is thickened, and there is a perivascular infiltration. Although giant cells and epithelioid cells are frequently present, the regular arrangement of a tubercle is absent. Vessels often persist in the areas of necrosis. Sclerosis in the healing portions of the lesion is intense and appears early. Even when all of these findings are present, the diagnosis can never be more than presumptive.

Of great value is an intradermal injection of *tuberculin*. In tuberculosis, this causes a local reaction.

The *Wassermann* is often positive, but when it is negative should be ignored.

Of most value is the *therapeutic test*, provided it is applied vigorously. Only mercury, bismuth, or arsphenamine should be employed. The frequent practice of administering large doses of iodide is wrong, because this drug simply causes infiltrations to disappear without being specific for syphilis.

The author concludes that the classical form of tertiary syphilis is rare; that the Lubet-Barbon form is the most common; and that certain lupoid forms have not only the aspect, but also the location, slow evolution, and absence of bone

destruction which are characteristic of lupus.

**Gastrointestinal Manifestations.**—Ten cases of syphilis are reported by A. G. Clasen (*Am J Syph* 14: 55, Jan., 1930) in which the chief symptoms were referable to the gastrointestinal tract, and he emphasizes the importance of looking for syphilis in the cases of patients presenting gastric symptoms which do not yield to the ordinary routine treatment for the secretory disturbances. He states that syphilis is frequently overlooked because it is not suspected.

The clinical picture of gastric neurosyphilis is often difficult to differentiate from that of true gastric syphilis. The gross gastric lesion of a syphilitic of the stomach, in both the hereditary and the acquired form, may be any one of the following:

1. Gastritis. This develops in all stages of syphilis, including the early secondary stage.

2. A circumscribed new growth, the gumma.

3. Diffuse gummatous infiltration and hyperplasia with thickening of the wall of all or a part of the stomach and the pyloric antrum. This form begins in the submucosa and extends to the mucosa and muscularis.

4. Gummatous plaques on the mucous surface.

Ulcers are generally multiple. They often extend upward along the lesser curvature and involve the greater curvature also to some degree. The fibrosis may be so pronounced as to form a callous ulcer. The ulcer may be the result of an obliterating endarteritis. Fibrous changes, such as scars, may lead to stenosis. They may also cause necrosis.

5. Gastric deformity, such as shrinkage of the stomach from gummatous infiltration of fibrous hyperplasia.

Except in the aorta and liver, syphilitic lesions can be identified only during the active stages of the infection.

In syphilis of the stomach, profuse hemorrhage, perforation, and fistula formation are rarer than in cases of benign ulcer, but hyperplastic chronic peri-gastritis is more common. In 50 per cent of cases of tabes, acute bleeding from the stomach is due to an ulcer rather than the tabes.

Cases may be classified according to symptoms as follows: (1) those suggesting gastric ulcer; (2) those suggesting gastritis and achlorhydria, (3) those of the diffuse fibrosis or scirrhus carcinoma type, (4) those showing retention and duodenal ulcer deformity, and (5) those with functional disturbances occurring as gastric crises.

In true organic syphilis of the stomach, the blood Wassermann test is generally positive, but gastric symptoms may be present in neurosyphilis in which the blood and spinal fluid Wassermann tests are negative. In a large percentage of cases of gastric syphilis, there are no positive x-ray findings indicative of syphilis. When an ulcer is present, it is almost invariably detected.

A positive history, in addition to positive blood and spinal fluid reactions, other signs of syphilis, and gastric manifestations, with corroborative x-ray findings in the case of a patient between 30 and 45 years of age, must be considered presumptive evidence of gastric syphilis.

Gastric syphilis was found in 89 of a group of 151 patients with gastric lesions and syphilis by P. A. O'Leary (Am J Surg 11:286 (Feb) 1931). These were selected from among approximately 25,000 patients with syphilis. The diagnosis was based on the combined results of prolonged thera-

peutic tests, histopathologic studies, morphologic changes in the x-ray characteristics, and restoration of gastric function. The demonstration of the existence of other evidence of clinical syphilis is not pertinent to the diagnosis of gastric syphilis. Of the 89 patients with gastric syphilis, 73 per cent had a positive Wassermann reaction of the blood as the only other evidence of syphilis, and 6 per cent had negative serologic reactions. The incidence of clinical signs of syphilis was almost as high in patients with gastric carcinoma (16 per cent) as it was in those with syphilis of the stomach (27 per cent).

**Syphilitic Celiacgia.**—The syphilitic origin of attacks of severe pain in the epigastric region is the subject of the investigations of J. Turriés (Arch d mal de l'app digestif 20:660 (June) 1930). In such cases the symptoms are cramps, sensations of twisting, burning, or of heaviness, often localized in the epigastric region and in general, without notable irradiation except toward the vertebral region. The pain element is not constant but has an alternating or undulating, rather than a periodic evolution. Vomiting, hematemesis or nausea is not observed. Salivation is sometimes noted, also slight constipation. The most constant symptom is pain, revealed on even slight pressure over the solar plexus. The general condition of the patient is satisfactory, a slight asthenia with irritability, and sometimes insomnia are also symptomatic. Although such cases have usually been variously diagnosed, the author finds that a complete detailed study will reveal, in addition to the painful epigastric syndrome, 2 others, *viz*, manifestations of (1) syphilitic infection, and (2) sympathetic dystonia. In the latter instance, the most common signs of vago-

sympathetic disequilibrium to be found are vasomotor (emotional and postprandial) disturbances and cenesthetic disorders. As to the syphilitic element, it is rarely great. Spirochetal infection, often latent or disguised, is revealed by various signs, such as anisocoria, inexplicable, long-standing refractory encephalitis, and modified reflexes. To prove that the disorders were of the etiology suspected, the author applied therapeutic tests. All digestive as well as the customary sedative treatments failed, while in all the cases considered in this present study, only spirocheticidal treatment gave certain and lasting results.

**COMPLICATIONS.**—An instance is reported by S. S. Greenbaum (Arch. Dermat. Syph. 21: 771 (May) 1930) of *hepatorecurrence* terminating in acute yellow atrophy in a patient who 3½ months previously received 4 small intravenous injections of neoarsphenamine for secondary syphilis. Intravenous injections of sodium thiosulphate, dextrose and sodium iodide and a single intramuscular injection of bismuth did not stay the progress of the disease. The use of the slow-acting drugs, bismuth and mercury, appears inadvisable in clear cut instances of hepatorecurrence. Arsenical therapy in maximum tolerated doses is not always contraindicated in patients with syphilis who develop icterus one or more months after the last treatment. This is especially true of those whose course of treatment had been insufficient.

**DIAGNOSIS.**—*Intact*, apparently healthy, tonsils have been examined by J. M. Tsherbakov (Vrach. dielo 14: 32 (Jan. 31) 1931) for the presence of *Spirochæta pallida*. He carried out 125 investigations on 100 persons, of whom 48 were men and 52 were women.

Among these 100 persons, 88 were affected with syphilis, 10 with various other diseases (herpes progenitalis, chancroid), and 2 healthy women were exposed to syphilis by syphilitic persons in their families. These 12 persons were studied not as controls only, but probably also for the discovery of latent forms of syphilis with a negative Wassermann reaction. The author's conclusions are as follows: (1) By means of constrictive hyperemia, *Spirochæta pallida* may be found in from 14 to 15 per cent of patients with latent secondary syphilis, whose tonsils are without macroscopic changes. (2) *Spirochæta pallida* may be found also on intact tonsils in persons with secondary syphilitic phenomena in other parts of the body (17 per cent). (3) The presence of *Spirochæta pallida* may precede the development of a pustular tonsillitis; this will help in cases that are difficult to recognize, as well as facilitate the finding of small pustules hidden in the depths of the tonsillar crypts. (4) It was impossible to find *Spirochæta pallida* 24 hours after the first administration of neoarsphenamine, whereas the action of mercury was much weaker and not so permanent. (5) By employing, as a routine, the method of passive hyperemia, enough material may be obtained in which besides *Spirochæta pallida*, *Spirochæta buccalis* and *Bacillus buccalis-maximus* may be found. This method is in all respects better and more convenient than the method of puncture of the tonsils.

An audiometric study of 792 patients on a general diagnostic service was made by D. W. Drury (Am. Otol. Rhin. and Laryng. 38: 625 (Sept.) 1929). An analysis of this group showed 81, or practically 10 per cent., exhibiting a curve characterized by a

marked lowering of auditory acuity at 4096 d v, and that in this group there was a surprising incidence of "putative or established syphilis." Emphasizing that the recognition of syphilitic auditory neuritis is of paramount importance as possible evidence of early cerebrospinal involvement, the author recommends the audiometer as the instrument of choice in the diagnosis of *incipient syphilis of the auditory nerve*. He further states that when this particular curve—the "dipper gap"—is encountered in a syphilitic, the aural damage is permanent, although the etiologic factor may be cured successfully.

*Edema* in patients with syphilis is discussed by G. Herrmann (Am J. Syph. 15:19 (Jan) 1931), who states that the clinical characteristic massive albuminuria of syphilitic nephritis is the initiating factor in the important biochemical changes, reduction of the serum albumen, and an attempted but futile compensatory rise of serum globulin that accounts for the accumulation of the edema. The hopefulness of the outlook of recognized and treated syphilitic nephritis as contrasted with the poor prognosis of nonsyphilitic types is stressed.

Syphilis as a cause of *delayed recovery from injury* is considered by J. Urbach (Med Klin 26:86 (Jan. 17) 1930). The case of a patient is reported in whom, following a severe crushing of the leg, 2 gummas developed in the injured area. At first they were refractory to treatment. Later, antisyphilitic therapy was instituted and this led to recovery. The contusion alone could not have caused the delayed recovery, but the tertiary syphilis, from which the patient was suffering, caused the development of the gummas, which yielded only to antisyphilitic therapy.

Two similar cases of late syphilis without other noticeable symptoms of syphilis and provoked and changed in appearance and course by *continued mechanical traumas* have been described by H. Haxthausen (Ugeskr f læger. 93:243 (Mar 5) 1931). In the one case the left palm was affected, while in the other it was the right. The Wassermann reaction was positive, and antisyphilitic therapy was followed by the disappearance of the lesions.

The *x-ray* appearance of certain bone and joint changes in syphilis, has been studied by R. Casazza (Radiol med 18:565 (May) 1931), who describes a number of these changes, calling attention to the great variety of such lesions and the difficulty of proving that a bone or joint disease in a syphilitic person is caused by the syphilis. The case reports are supplemented by x-rays.

The first case was that of a child 7 years of age, with hereditary syphilis. In the vault of the skull there was a rather soft area, the size of a quarter, which had an elevated border. Pressure on this area caused pain. The x-rays showed serious destruction of bone. None of the other bones of the skeleton was affected. The child was mentally defective. His mental condition and bone lesion improved greatly under treatment with *bismuth*.

The development of bone syphilis seems to depend on both a general and local factor. This was indicated by a case of acquired syphilis in a man of 25 years who showed distinctly productive lesions in the tibiae and distinctly destructive lesions in the superior maxilla. The difference is attributed by the author to a local factor.

In the case of a man 65 years of age, the bones of the skull and the distal ends of the bones of the forearms and legs



were thickened and enlarged, evidently as the result of the general action of the virus, and serious lesions were present in the kidneys and circulatory system

In syphilitic persons, trauma may cause localization of the syphilis in the bones. Illustrative cases are cited. Also cited are cases of joint lesions in syphilitic persons in which it was impossible to prove that the joint disease was caused by the syphilis. The author characterizes the joint disease in such cases as arthropathy in a syphilitic rather than as syphilitic arthropathy. However, he believes that in the cases cited, the preponderance of evidence indicated that it was syphilitic. As known syphilitic changes are not always corrected by specific treatment, this theory is not disproved by the fact that in some of the cases the condition did not react very well to antisyphilitic treatment.

J. S. Friedenwald (Am J Ophth. 13.943 (Nov) 1930) states that the occurrence of the ophthalmoscopic picture of *retinitis pigmentosa* as the result of a diffuse chorioretinitis in congenital syphilis is well known. In acquired syphilis, this condition is much less common, but its occurrence has been well recognized since the classical description by Forster. The latter, however, has no data as to the nature of the syphilitic disease in the patients, though he pointed out that diffuse chorioretinitis generally occurs late in the syphilitic infection, and is never associated with the primary or secondary stages. To the 2 cases reported by Forster, the author adds 3 more, 1 of which is as follows: Mr. A., 48 years old, was seen in February, 1926, complaining of failing vision, loss of weight and depression. Five months previously, the diagnosis of tabes with optic

atrophy had been made. Blood and spinal fluid Wassermann tests were positive. He had received a course of salvarsan and bismuth and had improved markedly. There was no history of familial lues, nor of retinitis pigmentosa, nor of a primary lesion. No night blindness.

Examination showed ptosis of the right lid, pupils dilated, irregular and unequal, not reacting to light, but slightly to convergence. Vision of right eye zero; left  $\frac{20}{30}$ . Ophthalmoscopic examination showed both discs to be pale, the right more than the left, disc margins irregular, retinal arteries markedly attenuated. Scattered throughout fundi were numerous irregular masses of pigment, some of typical crescentic form, overlying the blood-vessels. In addition, there was a great deal of fine pigment peppering, and numerous small white dots. There was slight analgesia about the nose, slight deafness in one ear, absence of knee and ankle jerk, loss of sense of position in the legs, a fairly typical tabetic gait, a positive Romberg test, and a slight tremor of the head and hands. The man was given a vigorous course of antiluetic treatment, but apart from a decrease in the amount of retinal pigment, the condition remained about the same.

The cases are of interest in that they present a type of optic atrophy associated with tabes which is favorably influenced by treatment. The association of the ophthalmoscopic lesion which is usually characteristic of congenital lues with tabes and paresis in acquired lues indicates that the nature of the bodily reactions (allergy and immunity) to the spirochete in late neurosyphilis resembles that found in congenital lues. Finally, it is of special interest to note that under treatment the amount of

retinal pigmentation in these cases shows a decided decrease. It must be concluded then that, once the invasion of the pigment into the retina has been stopped, the normal processes of transport and repair tend to remove the pigment which has already been laid down in the retina.

J. P. Kosman (Vrach dielo 13 1418 (Oct. 31) 1930) states that the recognition of syphilis of the *internal organs* is at times a difficult task, for many patients do not disclose that they have syphilis or they even forget about it if the primary infection was of a mild nature. As an illustration of this, the author reports the case of a woman, aged 49, who was brought to the clinic in a grave condition. The latter was diagnosed as cancer of the stomach. The past history revealed many, mostly so-called rheumatic ailments for which the patient was treated for years with no apparent results. Most of her complaints in the past were in relation to the large joints and spine. Lately she had vomited persistently. Physical examination revealed an enlarged liver and spleen extending far down from the border of the lower ribs. The liver was tender and hard on palpation. The edge of the spleen was smooth. A tumor with an uneven surface could easily be felt between the liver and the spleen. All these observations, as pain in the abdomen, enlarged spleen and liver, the presence of a neoplasm that could be felt in the region of the stomach, as well as the nervous and toxic symptoms, made the author think of cancer of the stomach and liver, with metastases to the brain. On the other hand, the multiplicity of bone and joint involvement with characteristic night crises were in favor of the diagnosis of syphilis. A cautious and slow antisyp-

ilitic treatment was established and in a remarkably short time the patient began to show signs of rapid improvement. Vomiting ceased entirely and the tumor in the stomach region became less and less noticeable until it disappeared. This case is of interest because, notwithstanding the numerous viscera involved in the syphilitic process, the aorta and the rest of the cardiovascular system were not endangered at all. There was a complete picture of syphilis of the bones and joints, the brain, the stomach and the retroperitoneal lymph nodes, as well as of the liver and spleen.

In a series of 179 cases of cutaneous syphilis studied by S. Irgang and A. M. Sala (Arch Dermat and Syph 21:552 (Apr) 1930), 25 per cent showed a positive direct delayed *van den Bergh reaction*. It occurred in 17 per cent of patients with secondary syphilis; 24 per cent with tertiary syphilis, and 4 with initial lesions. In all but 4 of 45 patients with positive van den Bergh reactions, the icterus index was above 6, and in these the results ranged between 4 and 6. In many of their apparently normal cases, the icterus index was above 6. In 12 per cent of 134 cases with negative reactions, the van den Bergh reaction became positive while the patients were under treatment; clinical jaundice, however, did not develop in any of these. Only 10 per cent of the 20 patients with positive reactions who were receiving from 4 to 8 treatments developed clinical jaundice, in spite of a maximum therapeutic dosage. In 35 per cent of the positive cases, the reaction became vegetative during treatment.

M. Tièche (Schweiz med Wchnschr. 59:1097 (Nov. 2) 1929) asserts that there are 2 forms of *syphilis d'emblée*, i.e., a *hematogenous* and a *lymphog-*

*enous* The hematogenous type develops after blood transfusions if the donor has syphilis. The lymphogenous type becomes manifest in inflammations of the inguinal lymph nodes. The author gives a detailed description of 2 cases of the lymphogenous form. Although *syphilis d'emblée* is characterized by the absence of a primary lesion, the author thinks that a small, perhaps microscopic, initial sore exists, but that it is not noticed. He stresses that patients with inflammations of the inguinal lymph nodes should be kept under careful observation for several weeks, even if other symptoms of syphilis are not present. If the serologic test at first gives negative results, it should be repeated from time to time. In order to prevent the hematogenous form of *syphilis d'emblée*, the author states that persons who have had syphilis should never act as blood donors. A negative Wassermann reaction is not always sufficient proof for the absence of syphilis. Persons supplying blood should be requested to sign a statement that they have never had syphilis.

N. N. Barshar (Vrach. Gaz. 9:672 (May 15) 1931) examined for *Spirochæta pallida* the punctate of lymph nodes that were nearest to the seat of the chancre. Eighty-five cases of syphilis were investigated, among them 42 of primary infection, 15 of early secondary syphilis, 9 of recurrent secondary syphilis, and 16 cases suggestive of chancre. The author describes in detail his technic and the method of differentiation between the true *Spirochæta pallida* and the pallida-like saprophytic spirochetes. In 42 cases of primary active syphilis, *Spirochæta pallida* was found in the punctate of the lymph nodes 28 times (66.7 per cent.). In the tissue fluid aspirated from the ulcers of 40 persons

with early secondary syphilis, *Spirochæta pallida* was found in the punctate of 7 (40 per cent.), and among 19 cases of recurrent secondary syphilis, it was observed in 4 (44 per cent.). In 16 persons who were suspected of having primary sclerosis, the examination of their punctate as well as of the aspirated fluid (from the ulcers) gave negative results. The diagnosis was correct in all cases except 1, because it was verified by further clinical observations and by the serologic observations. The author concludes by emphasizing that the punctate of the lymph nodes is an excellent object for the study of such an important problem as the morphology of the exciting agent of syphilis.

For demonstrating spirochetes in all tissues except that of the central nervous system, A. S. Warthin (Brit. J. Ven. Dis. 5:255 (Oct.) 1929) believes the *starch gelatin modification of the Warthin-Storry silver agar method* is more convenient and specific, and yields more uniform results with a higher percentage of positive demonstration of the organism in association with the characteristic histological lesions of syphilis.

**Serodiagnosis.**—Despite technical improvements of the past several years resulting in an increased sensitiveness of serum tests, J. A. Kolmer (Am. J. Syph. 15:383 (July) 1931), believes that all complement-fixation and flocculation procedures are still capable of yielding falsely negative reactions and especially in some cases of extremely latent syphilis, with especial reference to late congenital or prenatal syphilis of children and syphilis of child-bearing women. There is still room for a further increase of sensitiveness, but this is to be carried only so far as is consistent with specificity, since it is a simple matter to make the highly regrettable mis-

take of increasing sensitiveness to the point at which falsely positive reactions occur.

It is better to fail in the diagnosis of an occasional case of syphilis than to run unnecessary risks of making a false diagnosis. The basis of this thought and practice is the fact that the serum tests for syphilis should possess only the maximum of sensitiveness consistent with specificity. And with this in mind, simplicity of technic, along with economy of time and materials, should be regarded as of secondary importance only. The general result is that the serum diagnosis of syphilis and the dependence on serologic tests as guides in treatment are best served at present by 2 or more procedures, one of which should be a Wassermann test of proved sensitiveness and reliability.

The results of comparative investigations on 15 different serodiagnostic methods in the examination of 944 specimens of blood (502 from patients with known syphilis) and 102 specimens of spinal fluid (90 per cent from patients with syphilis), carried out in the second laboratory conference of serologists, held at Copenhagen in 1928 are reported by T. Madsen and J. R. Morch (*Ugeskrift for Læger* 91:961 (Nov. 7) 1929). Precipitation reactions were found to be superior to even the best Wassermann methods in sensitivity and equal in specificity. The application of both a *precipitation* and a *Wassermann reaction* is advised in the examination of all specimens of blood and spinal fluid.

R. L. Kahn (*Urol. and Cutan. Rev.* 34:1 (Jan.) 1930) noted that 5 requirements for optimum precipitation are observed in syphilis: optimum concentration of antigenic lipoids in the antigen, proper physical state of antigen suspension; correct quantitative relation be-

tween serum and antigen suspension, shaking—as a probable aid in hastening collision between the interacting particles, while total dilution of a suspension-serum mixture should be a minimum. The Sach school believes that serum reactions in syphilis fall under immunity reactions. The Landsteiner school believes that there is not sufficient experimental evidence for this view. This brings us to the practical application of serum reactions in syphilis. A positive reaction in a case for diagnosis is generally accepted to mean active syphilis and to indicate therapy. The significance of a positive reaction after intensive therapy, however, is still a matter of opinion among different workers. Some, especially Wile, have for a long time contended that a positive serologic reaction may be an expression of immunity in syphilis to the same degree that a positive Widal reaction may be an expression of immunity in typhoid. Thus, there is a difference of opinion today as to the significance of positive serologic reaction in relation to syphilis therapy. Further experimental evidence is necessary before the immunological character of these reactions will be fully established. In addition, it is hoped that the laboratory will develop some biologic criteria for cure in syphilis.

A close agreement of the results of the *Wassermann* and the *Kahn tests* as performed at the Army Medical School, was found by E. B. Vedder (*Porto Rico J. Pub. Health and Trop. Med.* 6:194 (Dec.) 1930). In some cases the Wassermann test gives a higher number of units than the Kahn test, and *vice versa*, but the discrepancies have so far involved differences only in the reading of one tube or dilution. Since in this work each succeeding tube contains only half as much serum as the preceding, it

seems probable that, by using many more tubes and diminishing the amount of serum used in the 2 tests by tenths instead of halves, a still closer approximation of the results would be obtained. This involves altogether too much labor and too much serum to be practicable for routine work. It is desirable to avoid reporting the 2 quantitative tests separately. Since there is such close agreement and since both tests are highly specific, especially in dilutions at which by no possibility can there be false positives, the plan is advocated of averaging the results of the 2 tests and reporting the results in syphilitic units. According to this system, if the Wassermann test shows 4 units and the Kahn test 10 units, this would be reported as 7 syphilitic units, 80 Wassermann units and 40 Kahn units as 60 syphilitic units. This suggestion has the merit of combining the results of the Wassermann and the Kahn tests, expressing this combined result in a strictly quantitative manner as syphilitic units, which will be more specific and delicate than the units of either test used separately.

M. A. Lyons (Arch Dermat and Syph 23:317 (Feb) 1931) performed the *Wassermann*, *Kahn* and *Vernes* flocculation tests, on identical specimens for blood serum. Standard technics were followed for each test. He noted that serologic results on identical specimens of serum from patients known to be nonsyphilitic agree, whereas those from syphilitic patients who have been treated disagree. The Vernes flocculation test and Kahn precipitation test may give positive results before the Wassermann test in early primary syphilis. Only slight disagreement existed in cases of primary and early secondary syphilis. Very close agreement existed in secondary syphilis. Tertiary cases of syphilis

showed marked disagreement, owing probably to treatment. Serologic results on identical specimens of serum following the provocative procedure showed that the Vernes flocculation test and the Kahn precipitation test gave positive reactions more frequently than the Wassermann test. Serologic results on identical specimens of serum from congenital cases of syphilis showed marked agreement. The Wassermann and the Vernes tests were more strongly positive than the Kahn tests. It is evident that more than one test, including the Wassermann, is indicated as a guide in the treatment of syphilis.

Comparative examinations by the *complement-fixation* and *precipitation-flocculation* tests were made by L. C. Todd (South Med J 22:1070 (Dec) 1929) on 7266 patients, with an average agreement between the 2 systems of 98.06 per cent. A clinical comparison between the *Kolmer-Wassermann*, the *Kline* and the *Hinton* tests in the examination of 728 patients showed that there was an agreement in all 3 tests of 96.43 per cent. There was an agreement between the Kline and Hinton tests of 99.45 per cent. There were no proved false positive reactions. The Kline antigen has proved superior in several important phases of diagnosis to the Kahn antigen. The Hinton glycerin-cholesterol precipitation reaction makes a superior check test for the complement-fixation test or for one of the other precipitation-flocculation tests. If the complement-fixation test is to be discarded, the Kline antigen in the Kahn tube test, checked by the Hinton test, makes a promising satisfactory serologic examination for syphilis.

N. Danbolt and E. Hårne (Norsk. mag. f. lægevidensk. 91:153 (Feb.)

1930) report that the results of the *Hinton* and *Wassermann* reactions agreed in 1110, or 92.5 per cent, of the serums examined and in 90 per cent of the cases of primary, secondary, tertiary and congenital syphilis. In secondary syphilis there was complete agreement. In treated syphilis, the results agreed in 86.95 per cent. of the cases, the *Hinton* reaction being somewhat more sensitive. In old latent syphilis, the *Hinton* test was more sensitive, a fact which may be advantageous in certain cases, as in cardiovascular disorders, but misleading in the treatment of distinctly nonsyphilitic conditions. The results tallied in 94 per cent of the 100 spinal fluids from patients with treated or untreated syphilis of the nervous system or diseases of nonsyphilitic origin. The method in the *Hinton* test is simpler than in other precipitation reactions, particularly *Kahn's* reaction.

The *d'Amato hemoclastic test* and also the *Wassermann* test were applied by G. Di Geronimo (*Riforma med.* 47:1554 (Oct. 12) 1931) in 27 cases, the results being absolutely the same with each test. He affirms, however, the practical advantage of the *d'Amato* test, owing to the simplicity of the technic employed.

A serologic test for syphilis, the so-called *S. R. reaction* is described by O. Sciarra (*Klin Wchnschr* 9:834 (May 3) 1930). He observed that under the ultramicroscope normal serum reveals small bodies that are homogenous in size and motility, whereas serum from syphilitic patients reveals bodies of various sizes that are either free or flocculated and that refract light. This observation led him to assume that these bodies and floccules are specific aggregates of syphilitic antibodies that react with auto-antigens. He found that when

ethyl alcohol is added the floccules disintegrate. Following this segregation between the antigens and the true antibodies, the latter fix the complement. This principle of reversibility is the foundation of the *S. R. reaction*. The *Wassermann* test is different, as in it the heterologous antigen reacts solely with the excessive antibodies that did not react with the auto-antigens present in the organism. The author describes the technic of the *S. R. reaction*. Either an absolute or a 96 per cent ethyl alcohol is required and sufficient complement to effect hemolysis of 1 c.c. of 5 per cent blood corpuscles. The author then discusses the reading of the reaction and stresses the absolute necessity of a control test. He recommends a combination of the *Wassermann* reaction with this new serologic test, and asserts that the latter is of great practical and theoretical value. It is more sensitive than the *Wassermann* reaction and it gives new scientific foundations for the diagnosis and treatment of syphilis.

All serologic reactions in syphilis may be viewed as colloid phenomena. According to R. Demanche (*Presse méd* 39:1070 (July 18) 1931), they constitute examples of the flocculation of one colloid, the lipid antigen, with another, the serum albumin. Recent researches tend to prove that the *antigenic function* is not due exclusively to albumins but to other organic substances, particularly the *lipoids*. It is known that antigenic function is manifested in 2 ways: (1) immunizing power—the formation of antibodies in the blood of a living person inoculated with antigen; (2) the reaction *in vitro*—the ability of the antigen to combine in the test-tube with the corresponding antibody and to react with it so as to fix the complement or



bring about flocculation. It has been found that a syphilitic liver, rich in spirochetes, is antigenic, whereas an alcoholic extract is not. However, the alcoholic extract combined with a foreign albumin will develop antigenic properties. Thus lipid, as well as proteins, possess antigenic properties, not only reacting with antibodies, but engendering these antibodies. The lipid-albumin complex contains the specific lipid together with the nonspecific protein. The activity of the lipid antigen depends not only on the chemicophysical state, but also on the proper colloid dispersion. In interpreting the reactions of colloid suspensions of lipoids, the rôle of the proteins must not be lost sight of. A secondary reaction due to the proteins may be so strong as to be manifested in the specific antigen-antibody reaction and bring about a nonspecific fixation of complement and flocculation. These pseudoreactions, due to the lack of stability of proteins and accompanying processes of cellular destruction, may be met in conditions such as pregnancy, tuberculosis, malignant tumors, severe pyrexia and cachectic states. It is the duty of serologists to prevent these pseudoreactions. This can be done only through much empiric experimentation.

**Differential Diagnosis.**—The differential diagnosis between *chancre* and *chancroid*, based on 1235 genital lesions studied at the United States Public Health Clinic at Hot Springs, is discussed by O. C. Wenger, A. A. Surgeon and H. O. Proske (Am J. Syph. 14: 313 (July) 1930). They believe that any diagnosis of a genital lesion unsupported by laboratory findings is questionable and that too much emphasis has been placed on clinical differentiation. A diagnosis of syphilis is

established in the presence of the following data: (1) positive darkfield for *Spirocheta pallida* and positive Wassermann test, (2) positive darkfield and negative Wassermann, (3) negative darkfield and a positive Wassermann. A case of this sort is not necessarily early syphilis, however, and the genital lesion may prove to be chancroidal. The diagnosis of chancroid can be established by (1) demonstrating the *Ducrey bacillus* by cultural methods, (2) the test of time, i. e., the inability to prove the presence of syphilis by repeated darkfields, gland punctures, and a series of Wassermann tests over a period of several months.

The authors state that it is difficult to obtain the organism of chancroid in pure culture because of the usual presence of secondary infection, both in the genital lesion and glands, at the time the patient is first seen. Furthermore, the *Ducrey bacillus* is seldom found in suspected lesions by smear preparation because of its tendency to give up its characteristic streptobacillus form as soon as suppuration and necrosis occur. Hence, in most cases of chancroid, the diagnosis must be made in retrospect after syphilis has been adequately excluded.

In the present study, a diagnosis of syphilis was established either by a positive Wassermann test, or a positive darkfield examination, or both, in 86 per cent. of the entire series. The remaining 14 per cent. constituted a difficult problem, for most of the patients were indigent and failed to cooperate in the necessary Wassermann follow-up. Twelve of the patients, however, later returned to the Clinic with evidence of syphilis. Some undoubtedly acquired a subsequent infection, but it is not likely that all the members of the group did so.

J H Stokes, H M Cole, J E Moore, P A O'Leary, T Parran, Jr and I S Wile (Ven Dis Inform 12 55 (Feb) 1931) have studied 5952 cases of early syphilis from their 5 respective clinics to ascertain the frequency, infectiousness, time and appearance, localization and morphology of *relapse*. Among these, 360 cases of mucocutaneous relapse and 40 supposed reinfections were thus brought to light, showing that relapse is one-fifth as frequent as chancre and consequently more easily ignored by patient and contact. Some of the more important conclusions of the paper are as follows: (1) the proportion of relapse is less in cases seropositive in the primary stage at the onset of treatment or in florid secondaries when they began treatment in the first year of their disease than in cases which are seronegative at the outset, (2) 68.6 per cent of mucocutaneous relapse were extragenital and 31.4 genital, (3) 62 per cent of relapse lesions are potentially infectious; (4) mucocutaneous relapse appears (91 per cent) in the first 2 years after treatment and 85 per cent of it occurs in the first 2 years of the disease, (5) arsphenamine-mercury therapy is followed by 9.6 per cent of relapse as compared with 3.6 per cent under arsphenamine-bismuth therapy; (6) the proportion of mucocutaneous relapse is greatly reduced after the ninth to the fifteenth arsphenamine injection, (7) the criteria for the acceptance of reinfection are reviewed and none in the present supposed series of reinfections are found to be completely acceptable. A small proportion only satisfy even moderately strict requirements.

**TREATMENT.**—It is important to stress the necessity of intensive treatment as early as possible in syphilitic in-

fections. No single plan of treatment has been agreed upon, but the combination of **arsphenamine** with **mercury** or **bismuth** should be used.

**Arsphenamine; Mercury.**—The routine treatment of early syphilis suggested by H B Decker (J Med Soc New Jersey 24 681 (Dec) 1927) is as follows: **Neoarsphenamine** 0.6 Gm (10 grains) intravenously, a second injection on the fourth, and a third on the eighth day. These injections are continued at 4- to 7-day intervals until 6 are given. One week after the sixth dose of neoarsphenamine, 1 grain (0.065 Gm) of **mercury salicylate** is injected intramuscularly. This is repeated at weekly intervals until 12 injections have been given, after which the patient rests for 4 weeks. After the rest period the neoarsphenamine is given at weekly intervals for a period of 36 weeks. Following this, the patient rests and Wassermann tests are done each month for the first 3 months, then at the fifth, eighth and twelfth months. Some time between the eighth and twelfth months the cerebrospinal fluid is examined. If at any time the Wassermann becomes positive or the cerebral spinal fluid abnormal, a course of 18 treatments is repeated. The patient is instructed to report each year for physical and serological examinations.

The main reasons given by E. T. Burke (Lancet 1 1127 (May 23) 1931) for his adoption and teaching of the *alternating method* of treatment of syphilis are the following:

1 Under the concurrent regimen, when arsphenamine and mercury were exhibited simultaneously, it was found necessary to interrupt treatment after the first 8 or 10 weeks in order to prevent the patient from showing signs of intolerance. An interval of from 2 to

4 weeks had to be allowed in which no therapy was given, so that the patient could recover from the toxic effects of the remedial agents administered. During this time the parasite was permitted, unmolested, to entrench itself in deep seated visceral structures, chiefly in the cardiovascular and central nervous systems. It, therefore, seemed more logical to try to arrange therapy so that rest periods were abolished and so that the parasite would be continuously subjected to an intense chemo-therapeutic bombardment. This could be done only by exhibiting the drugs in alternate courses.

2 It was found that under concurrence there were many patients who developed jaundice, nephritis and exfoliative dermatitis. This was considered to be due probably to the double assault on the hepatic, renal and cutaneous system. On changing over to the alternating system, the incidence of these complications, especially nephritis, almost reached the vanishing point.

3 Under the concurrent method, many patients were found to have become drug resistant or Wassermann-fast. This was thought to be due to the development by the spirochete of an immunity to the action of the remedial agents. It seemed natural, therefore, to reason that it would be better to administer the drugs in separate series, so that no sooner did the parasite threaten to develop a resistance to one agent, than a new weapon was brought into action, and when the efficacy of that drug began to wane, a change was made back to the original one or to another new one, if one was available. Experience has shown this reasoning to be correct, for, since the adoption of the alternating method, drug resistance and Wassermann-fastness have ceased to appear as practical difficulties.

4 A study of the mode of action of arsphenamine and of bismuth (for mercury has been discarded as being insufficient and a mere waste of time) also forced the author to give up concurrent treatment. Arsphenamine and bismuth do not act directly on the parasite. When injected into the body, they stimulate the tissues to produce toxalbumins (arsenoxyl and bismoxyl) that are lethal to *Spirocheta pallida*. In other words, the arsphenamine and the bismuth are the raw materials supplied to the body that produces the finished article capable of destroying the parasites. The manufacture of these proteoarsenic and proteobismuth combinations inevitably throws some strain on the producing tissues of the patient. When raw materials are exhibited simultaneously, twice as great a load is cast on the productive mechanism as when only one is given. The tissues are thus, under concurrence, more easily exhausted, and may finally cease altogether to produce the lethal toxalbumins. This results in drug resistance and Wassermann-fastness.

5 Many patients who formerly had become Wassermann-fast under concurrence have been treated during the past 10 years by the alternating method. A large proportion of the cases, as a result, became permanently negative.

6 Under the alternating method there is a saving in time and in the amount of remedial agents necessary to cure a patient with early syphilis.

The *prenatal treatment* of syphilis is discussed by U. J. Wile and J. W. Shaw (J. A. M. A. 95:1791 (Dec 13) 1930), who state that **salvarsan** is well tolerated by pregnant women, and there is no apparent relationship between the intravenous administration of the drug and miscarriage or abortion. Prenatal

treatment modifies definitely the syphilitic changes in the placenta. Regardless of the absence of clinical or serological observations, it seems wise to treat babies born of mothers in whom the syphilis is early, to supplement the prenatal treatment of the mother. The results of the investigations of E. Gottlieb and N. I. Nissen (*Ugeskrift for læger* 92 1039 (Nov.) 1930) show that the use of **arsphenamine** does not increase the tendency to syphilitic conditions of the cardiac vessels and also indicates that it protects against their development. Long-continued treatment with **mercury** likewise seems to afford some protection against the development of late syphilitic disease.

Thirty-two patients with Wassermann-fast syphilis were treated by J. L. Grund (*New England J. Med.* 203 76 (July 10) 1930) with **sulpharsphenamine**. In only 1 case were the serologic observations favorably influenced. The negligible quantity of cases favorably affected is indicative of the fact that the change in the 1 single case was probably coincidental and bore no relation to the administered drug. Cutaneous disturbances directly attributable to the administered **sulpharsphenamine** were noted with much greater frequency than is customarily apparent in cases treated with other antisyphilitic arsenicals. Pain invariably accompanied the intramuscular administration of **sulpharsphenamine**. It was not infrequently severe and enduring. In addition to its lack of effectiveness in Wassermann-fast syphilis, the features just mentioned indicate that if **sulpharsphenamine** is used at all, it must be with caution and with awareness of its possible untoward effects.

**Mercurial Ointments**—H. N. Cole, N. Schreiber, and T. Sollmann (*Arch*

*Dermat. and Syphil.* 21 372 (Mar.) 1930) believe that their research proves that the absorption and excretion of mercury after inunction is directly dependent on the concentration of the metal in the base. Mercury in an oleate base does not seem to be much more absorbed than in the ordinary benzoinated lard and suet base. Colloidal mercury ointments show no greater excretion of mercury than official mercury ointments of equal concentration in benzoinated lard. Salivation is possibly more frequent with the colloidal preparations. Fifty per cent mercury in a stiff petroxolin base shows no especial difference in the excretion of mercury from that when simple inunction of 50 per cent. mercurial ointment is used. Massive or intensive weekly inunctions of a 30 per cent mercurial ointment, total 9 Gm. (2¼ drams) of metallic mercury, give an equal or higher excretion of mercury than the simple daily use of 50 per cent mercurial ointment or 50 per cent. clean ointment, or daily intramuscular injections of mercuric bromide.

**Bismuth Preparations.**—The advantages of bismuth therapy over the **arsphenamine** treatment of syphilis is discussed by A. Schwartz (*Presse méd.* 39 809 (June 3) 1931). He states that he has used **liposoluble bismuth** preparations in all stages of syphilis and obtained most favorable results, which were corroborated by many well-known syphilologists. He questions the correctness of many practitioners who still prefer the use of the **arsphenamines**, regardless of the fact that with bismuth therapy all syphilitic lesions are cured much faster than with **arsphenamine**. In submitting his questions for consideration, the author does not propose to abandon the **arsphenamines** entirely.

He suggests that they be kept in reserve for exceptional cases in which bismuth fails, because the use of the arsphenamines is still accompanied by a certain risk. Only in exceptional cases is it right to submit the patients to the dangers of intravenous injections of arsphenamine. Every one who employs these injections will not deny that, even with the most scrupulous precautions, there is a possibility of encountering a grave accident, sometimes a fatal one. Furthermore, by employing liposoluble bismuth in the beginning of the treatment, a harmless and energetic therapeutic measure, remarkable results are obtained in the great majority of cases without danger to the patient.

Although bismuth is adopted by syphilologists as a substitute superior to mercury, little is said of the action of the various preparations of bismuth in syphilis. It is a well-established fact, according to S. Lomholt (Brit. M. J. 2:887 (Nov. 16) 1929), that a complete cure is attained only after a prolonged course of bismuth therapy. The aim of the therapy should be to introduce into the organism the largest possible quantities without intoxication. The elimination of the metal is rather slow. Intensive bismuth treatment should not be continued long. It is essential that the preparation should be uniformly absorbed. Oral and cutaneous administration are unreliable. Intravenous injection is rather dangerous. The subcutaneously injected bismuth is irregularly absorbed and may cause an abscess. Intramuscular injection is the preferred method. In the different preparations the metallic bismuth content alone is important, provided that the organism can dissociate the bismuth. All bismuth preparations injure the muscle tissue, causing the formation of a

small necrosis, which is gradually replaced by granulation tissue which more or less prevents the absorption of the preparation used. Watery solutions are effective but rather painful when injected, and the administration has to be repeated frequently. Oily solutions are painless but rather slowly absorbed. Among the various preparations used in oil, **bismuth salicylate** seems to be one of the best. If watery solutions are selected for administration the preparation preference should be given to compounds of restricted solubility. The **oxychloride of bismuth** is one of the best preparations for watery solutions. With particles of a size of 3 to 5  $\mu$ , it is almost painless and very powerful. If the absorption of the preparation is complete, the daily dose of bismuth metal may be fixed at about 0.5 mg. ( $\frac{1}{120}$  grain) per kilo. ( $2\frac{1}{3}$  pounds) of body weight.

The author used the following method of treatment in 152 cases with fresh syphilis without a single relapse. **Neoarsphenamine**, in doses of 60 to 70 cg. (10 to 11 grains), was given in a series of 5 to 6 intravenous injections and **bismuth oxychloride** in watery suspension, in doses of 15 to 20 cg. ( $2\frac{1}{2}$  to 3 grains), in a series of 8 to 10 intramuscular injections. The total number of about 18 neoarsphenamine and 60 bismuth oxychloride injections are given within a period of about 2 years. At the end of treatment of the 152 patients, only 2 showed a positive Wassermann reaction, 7 a doubtful and 143 a definitely negative test. Each case should receive individual consideration during the treatment.

For the past 9 years, C. Levaditi (Am. J. Syph. 14:156 (Apr.) 1930), Fornier and their associates have used bismuth in the treatment of syphilis

practically to the exclusion of all other drugs. Levaditi reaffirms the principles previously reported by him, which include (1) Bismuth has a curative and preventive action in early and late syphilis, (2) it causes the rapid disappearance of the spirochete from the early lesion, (3) it sterilizes the lymphatic glands, (4) it causes a favorable modification of the reactions of the blood and spinal fluid; (5) it exercises a profound and lasting curative action in syphilis—principally because of its delayed elimination, and (6) it acts where arsenic fails (in arsenic-resistant cases). To these earlier principles, Levaditi has added (7) Bismuth is superior to arsenical therapy with the exception of the prompt sterilizing qualities of the intravenous arsphenamine, (8) it is absolutely innocuous, provided neither intravenous bismuth nor the water-soluble intramuscular preparation is used; (9) it is superior in its therapeutic properties to mercury, and (10) bismuth therapy is efficacious not only in acquired syphilis, but also in the hereditary and congenital form.

The author devotes considerable space to a discussion of the proper preparation and salt of bismuth to be used. He believes that the most efficacious type is either the insoluble bismuth salts in oil suspension or the fat-soluble compound. The main criteria in the choice depend on the formation of bismuth deposits in the body with the subsequent formation of bisoxyl, and the actual amount of metallic bismuth contained in the preparation. He names 3 classes of bismuth compounds as meriting consideration: (1) The iodoquinine salts of bismuth; (2) the oxides or oxycarbonates of bismuth, and (3) the fat-soluble derivatives. He favors the use of the latter type of bismuth compound and

particularly **a-carboxethyl; b-methylnonoate of bismuth (biliposol)**. The bismuth content is 0.04 Gm ( $\frac{2}{3}$  grain) per 1 c.c. (16 minims) of the oily solution. Experimentally, the curative dose varies from 1 to 2 mg ( $\frac{1}{16}$  to  $\frac{1}{32}$  grain) of metallic bismuth to the kilogram ( $2\frac{1}{2}$  pounds) of body weight. The sterilization of local lesions is prompt and its effect on the Meinicke reaction is comparable to the arsphenamines. Clinically, the salt is employed in bi-weekly intramuscular doses of 2 c.c. ( $\frac{1}{2}$  dram) of the oil in a series of from 10 to 15 injections. The salt is well tolerated and evidence has been gathered that the radiographic bismuth shadows are more diffuse and less opaque than those of insoluble oily suspensions of bismuth. Renal elimination commences rapidly after the injection and is demonstrable up to  $1\frac{1}{2}$  to 2 months after the cessation.

J. A. Kolmer (*Ibid* 15:190 (Apr) 1931) states that **basic bismuth camphocarboxylate** is a new compound of bismuth soluble in oil and more rapidly absorbed from the muscles with less local reaction than insoluble compounds of bismuth. It has proved of particular value for the bismuth treatment of children and especially of adults who do not bear well, or suffer excessively from, pain following intramuscular injections. Its maximum single tolerated dose by intramuscular injection in rats is about 0.3 Gm (5 grains) per kilogram ( $2\frac{1}{2}$  pounds) of weight. As the adult dose is 0.1 Gm ( $1\frac{1}{2}$  grains), or about 0.0015 Gm ( $\frac{1}{40}$  grain) per kilogram ( $2\frac{1}{2}$  pounds), the amount ordinarily administered at one time is about 200 times less than the maximum tolerated dose for the rat.

The intramuscular injection of 10 to 20 doses of 0.0015 Gm ( $\frac{1}{40}$  grain) of



basic bismuth camphocarboxylate to the lower animals at intervals of 3 or 4 days has produced no discoverable microscopic changes in the kidneys, liver and other organs. Single doses of 0.4 to 1.5 Gm (6 to 23 grains), per kilogram ( $2\frac{1}{3}$  pounds) have produced tubular nephritis of varying severity in rats. Intramuscular injections have produced less necrosis of muscle and more diffuse local reactions in guinea-pigs than injections of an insoluble salt of bismuth. They have also produced remarkably little pain and local reactions in children and adults and are to be particularly recommended from this standpoint. Constitutional reactions or evidences of renal irritation have not been observed following a dose of 2 cc (32 minims) of solution (0.1 Gm— $1\frac{1}{2}$  grains) for adults and 1 cc (16 minims) (0.05 Gm— $\frac{3}{4}$  grain) for children. This preparation is without demonstrable trypanocidal activity, as is true of bismuth compounds in general. The minimum curative single dose for rabbits with acute testicular syphilis has been about 0.02 Gm ( $\frac{1}{3}$  grain) per kilogram ( $2\frac{1}{3}$  pounds) of weight, giving a chemotherapeutic index of about 15. It has caused the disappearance of *Spirocheta pallida* from penile chancres less rapidly than bismuth arsphenamine sulphonate and has produced the healing of primary and secondary lesions less rapidly than arsphenamine and neoarsphenamine. It was absorbed from the muscles of guinea-pigs more rapidly than an insoluble salt of bismuth.

Kolmer found that basic bismuth camphocarboxylate possesses therapeutic effectiveness in the treatment of syphilis, and he particularly recommends it for the treatment of chronic, acquired and prenatal syphilis, because it is practically painless, produces little or no

local reaction, and is remarkably free of constitutional reactions.

The immediate results are reported by D. C. Smith and J. W. Baker (South M. J. 23:188 (Mar.) 1930) of the treatment with **sodium bismuth tartrate** of 6 cases of syphilis with cutaneous manifestations. The toxicity and reactions following intramuscular injections are said to be minimal. The authors feel that this preparation is spirocheticidal and has a curative effect.

**Bismuth Arsphenamine Sulphonate (Bismarsen)**—J. H. Stokes, T. H. Miller and H. Beerman (Arch. Dermat. and Syph. 23:624 (Apr.) 1931) and his associates believe that the field of greatest promise for bismuth arsphenamine sulphonate is that of early syphilis. In this field they commend its use in continuous treatment, without rest intervals, 2 injections a week, to as near 40 injections as possible. Attention to technical detail, while it need not be excessive, facilitates the use of the drug by this method. **Massage and hot applications** are items of importance and should not be regarded as beneath the notice of the therapist. The relative simplicity of administration, the comparative rarity of complications, the low proportion of relapse in the most significant phase of the disease, from the standpoint of both the individual and the public health, all seem to point to bismuth arsphenamine sulphonate as a practitioner's advance in the control of syphilis.

A careful study of 152 patients suffering from all types of syphilis who were placed on bismarsen therapy, was made by C. H. de T. Shivers (*Ibid.* 22:462 (Sept.) 1930). The use of 20 injections of **neoarsphenamine** of 0.6 Gm. (10 grains) each and 20 injections of **potassium bismuth tartrate** of 0.1

Gm. ( $1\frac{1}{2}$  grains) each was more efficient than bismarsen alone in sterilizing patients who have *early syphilis*. Therefore, in this stage, the latter drug should be used only as a second course, thus a larger percentage of patients will be completely sterilized and at the same time complications which frequently occur during the second course of intravenous treatment will be avoided. Those in whom bismarsen may be the only drug used for early syphilis are old people, debilitated persons and patients in whom syphilis is complicated by another disease. In *late syphilis*, bismarsen is more frequently the drug of choice when it is desired to administer arsenic and bismuth, as the reactions are much fewer and consequently the danger less. The clinical improvement and effect on the Wassermann reaction have been very favorable. The clinical effect of this drug in cerebrospinal syphilis, especially of the acute meningeal type, has been most striking.

Bismuth arsphenamine sulphonate (bismarsen) combines the advantages of intramuscular and combination therapy, according to J. A. Kolmer (*Ibid* 21:394 (Mar) 1930) who reports his experimental and clinical observations. In 4 cases of primary syphilis the intramuscular injection of 0.2 Gm. (3 grains) of bismarsen caused the disappearance of spirochetes in from 36 to 120 hours. These lesions, however, as well as the lesions of the skin and mucous membrane of the secondary stage, disappeared more slowly than is ordinarily observed after the intravenous injection of from 0.4 to 0.6 Gm. (6 to 10 grains) of arsphenamine or 0.9 Gm. (14 grains) of neoarsphenamine. Bismarsen has proved especially valuable in the treatment of chronic syphilis because (a) it affords a means of avoiding Jarisch-

Herxheimer reactions, (b) it exerts greater spirocheticidal effects than mercury or insoluble bismuth compounds; (c) it has the advantage of safely testing the tolerance of patients for arsenic who have previously had arsenical treatments or accidents, (d) it has tonic effects; and (e) it represents a true form of combination chemotherapy. Bismarsen would appear to have a special field of usefulness in the treatment of *congenital syphilis*, particularly in children of 4 years of age or less to whom intravenous medication may not be given. Bismarsen has yielded encouraging results in the treatment of *pulmonary spirochetosis* and in severe cases of *Vincent's angina*.

P. A. O'Leary and L. A. Brunsting (New York State J. Med. 30:1223 (Oct. 15) 1930) have had 4 years of experience in the use of bismuth arsphenamine sulphonate (bismarsen) in the treatment of syphilis, particularly of the acute phases of the disease. Of the 167 patients with *acute syphilis* who were started on treatment, 64 completed a series of at least 30 injections, but only 30 of these patients have been observed recently enough to warrant statistical study. Of the latter, 21 have not shown evidence of clinical or serologic relapse, whereas 9 have manifested neurorelapse in the form of a symptomatic neurosyphilis. Six patients with chancre, whose treatment was started while the Wassermann reaction of the blood was still negative, apparently are "cured." Of 14 patients who presented sero-positive primary syphilis when treatment was started, 7 have withstood the test of observation and the condition of 7 has relapsed in one form or another.

None of the 9 patients who presented asymptomatic neurosyphilis when first seen with the signs of acute syphilis,

manifested improvement in the condition of the spinal fluid. It is thus evident that the incidence of relapse, particularly in the nervous system, following the use of bismuth arsphenamine sulphionate is higher than with other systems of treatment previously used for acute syphilis. In those in which injections of mercury were used coincidentally, no material decrease in the incidence of relapse was noted. In a smaller series of cases in which treatment has been administered more recently, decreasing of the intervals of time between the courses to 2 weeks, and giving a minimal of 40 injections, there has not been as yet any obvious change in the results of treatment.

The encouragement, drawn from the response in a limited number of cases, early in their experience with bismuth arsphenamine sulphionate, has not been substantiated by O'Leary and Brunsting by longer observation in a larger series of cases. That the drug has limited value in syphilotherapy is evidenced by the results of treatment in the seronegative stage of chancre. However, the frequency of neurorelapse has been sufficiently high to offset the results in this small group.

**Fever Therapy.**—C. C. Dennie, H. M. Gilkey and S. F. Paluka (Amer. J. of Syph. 15: 320 (July) 1931) show that the malaria parasite itself, or through some of its secondary action, is antagonistic to the presence of *Spirochæta pallida* and to the reactions that are produced by it, and that its use in syphilitic individuals causes the actual disappearance of hyperplastic or destructive syphilitic lesions. They do not advocate as a superior remedy the use of therapeutic malaria in preference to the arsphenamines, mercury, bismuth or the iodides. In early *acute interstitial*

*keratitis*, malaria therapy seemingly caused rapid disappearance of lacrimation, photophobia and circumciliary injection, and produced rapid clearing of haziness of the cornea. In old cases of chronic interstitial keratitis in which connective tissue is present in the cornea, no benefit would be obtained in the use of malaria. The haziness would remain unchanged. In *hyperplastic bone syphilis*, the action of malarial therapy was apparently decided. The superimposed bone disappeared quickly. In cases of periarticular infiltration of the knee joint the hyperplastic tissue disappeared and function was restored. In resistant *malignant skin syphilis* in which all other methods had failed, a remarkable recovery was secured in a short time. Malaria does not, as a rule, change a persistently positive blood Wassermann reaction to a negative one. This fact has been observed in both congenital and acquired syphilis. In 2 cases of resistant skin syphilis in which the lesions disappeared with malarial therapy, a slow recurrence of the skin manifestation became apparent in a few weeks.

The authors believe that malaria does not produce a clinical cure in any case of syphilis, but so raises the natural immunity forces of the body against the disease that the affected individual can combat his infection better after having malarial inoculation. The response to subsequent antisyphilitic remedies was better than it was before malaria was given. They, therefore, strongly advise that all persons with resistant or refractory syphilis, whether they are affected with the somatic or the central nervous system type, be given the advantage of subsequent antisyphilitic treatment.

**Thermotherapy.**—In an investigation bearing on febrile body temperatures as a possible adjunct treatment in

Wassermann-fast syphilitic patients, L D Cady and F H Ewerhardt (*Ibid* 13 313 (July) 1929) conducted a series of hot baths on 13 patients with syphilis. With 1 exception, all the cases were of the chronic type and designated Wassermann-fast. The bath temperatures varied from 104° to 107° F (40° to 41.6° C), at the outset, with subsequent bath temperatures of 104° to 111° F (40° to 43.8° C). The body temperature rose to 102.3° to 106° F (39° to 41.1° C) in 20 to 40 minutes. In general, the bath was continued at the highest tolerated temperature for 20 to 40 minutes. The pulse rate rose in proportion to the body temperatures. No serious adverse reactions were encountered. The authors present their data in the form of 13 complete histories and protocols with no general tabulation of results. Their investigations did not reveal any consistent evidence that hot baths were useful in Wassermann-fast patients. They believe that the serologic reactions were rendered more labile during relatively short periods of thermotherapy. The fact that there was an improvement in the patient's sense of well being and an apparent serologic response in a small percentage of their cases has encouraged the investigators to continue their studies on this mode of therapy.

**Quinine Bismuth Iodide.**—Good results were obtained by E P Fidanza (*Semana med* 2.1430 (Nov 14) 1929) in the treatment of primary and secondary syphilis by intramuscular injections of a proprietary preparation of quinine bismuth iodide, dissolved in water. The injection is given every other day and does not cause inflammatory or local reactions; it is painless and is well tolerated. The author asserts that the intramuscular injection of this

solution has a more rapid action than the oily or organosynthetic suspensions. In cases of greatly infiltrated chancre, he observed the disappearance of the spirochetes as early as the second day after the injection, and healing of the chancre resulted as early as 10 days after the injections were begun.

**Tellurium.**—A D Frazer (*Lancet* 2 133 (July 19) 1930) states that tellurium is a powerful antisyphilitic drug which would undoubtedly be more widely used but for the inevitable smell of garlic following its administration, and the fact that bismuth seems to act almost identically without producing this odor. There remains, however, one class of case in which tellurium might be useful, namely, the Wassermann-fast case, in which, in spite of the exhibition of arsenic and bismuth or mercury, the patient does not react serologically and lives with the possibility of recurrence of clinical manifestations of the disease hanging over his head. Seven Wassermann-fast cases were treated by the author with tellurium, 4 of which were favorably influenced. A course consisted of about 5 cc (1½ drams) of tellurium suspension given intramuscularly in 0.5 to 1 cc (8 to 16 minims) doses at intervals of from 5 to 7 days. A month's rest was then allowed before the Wassermann reaction was tested.

**Treparsol.**—E P Fidanza, J M M. Fernandez and E L Martinez (*Semana med* 2 286 (Aug 1) 1929) report on their use of treparsol in the Skin and Syphilis Clinic of the University of Rosario. They found the spirocheticidal action good in all stages of lues. Spirochetes disappeared from the lesions in from 3 to 4 days and the latter cleared up entirely. In the dosage used it is well tolerated. About 38 Gm. (1¼ ounces) are given over a period of 10

weeks, 2 Gm (30 grains) the first week, 4 Gm (1 dram) each following week. A month's intermission is then followed by a second course. In primary syphilis lesions healed in the second week. The Wassermann reaction appears to become negative about the fifth week. In secondary cases, the results are also favorable, the Wassermann becoming negative, as a rule, by the tenth week. In tertiary manifestations they claim to have obtained clinical improvement, but the Wassermann remained positive. In 4 cases of pregnancy of syphilitic women the offspring was free from syphilis; Wassermann negative. The only sequela observed was slight erythema following overdosage. Treparsol can be combined in mixed courses with bismuth and mercury.

**Treatment of Syphilis in Tuberculous Patients.**—From a study of the records of 1000 cases of tuberculosis M. Sullivan (Am J Syph. 15:37 (Jan) 1931) found the incidence of syphilis to be 11.6 per cent. From data presented, the following general rules may be formulated. If the syphilis is latent, the patient is old, or there exist such serious complications as chronic nephritis or heart disease, it is probably advisable to try first **general hygienic care** and if no improvement results, to begin antisyphilitic therapy cautiously. When the syphilis is active and also when it is influencing the severity of the tuberculosis, the syphilis should be treated. This is substantiated by the fact that general experience has shown that in all types of tuberculosis and syphilis there is (under antisyphilitic treatment) a higher percentage of improvement and a decrease in the death rate. The dosage should be at first 0.25 Gm (4 grains) of **neoarsphenamine**,

later increased to 0.4 Gm (6 grains). Never should more than 0.6 Gm (10 grains) of the arsenical be used, for, although smaller doses are well tolerated, patients treated with from 0.6 to 0.9 Gm (10 to 14 grains) of neoarsphenamine usually show an aggravation of the tuberculosis and often die. The treatment when once begun, however, must be carried out completely. **Mercury** and **bismuth** compounds should supplement the arsenicals. Iodides should not be used.

**Treatment of ocular syphilis** is very complicated, according to J. V. Klauder and H. F. Robertson (Am J Ophth. 13:285 (Apr) 1930) who also state that each case is highly individualized, so that the staff and resident ophthalmologists should collaborate in the treatment. **Potassium iodide** is used in all cases. **Sodium iodide** is given intravenously in *interstitial keratitis* and in *lesions of the oculomotor nerves*. **Mercury** is indicated when arsenicals are not well tolerated. **Bismuth** is highly regarded, especially for *interstitial keratitis*.

**COMPLICATIONS DURING TREATMENT.**—An unusual reaction following arsenical treatment of syphilis is reported in a case observed by N. Black (Canad M. A. J. 22:673 (May) 1930) which he considers was apparently one of *benzene poisoning* following 5 weekly injections of 3 Gm. (45 grains) of **neoarsphenamine**. The usual signs of arsenic poisoning were absent. In spite of vigorous treatment (4 transfusions, large doses of sodium thiosulphate, calcium lactate, reduced iron, and liver) the patient died with typical signs of bronchopneumonia. A postmortem examination showed, besides the bronchopneumonia, a liver moderately enlarged, a spleen smaller

than normal, petechial hemorrhages throughout the gastric and intestinal mucosa, and fatty degeneration of the marrow of the long bones.

*Jaundice* during antisyphilitic treatment has been investigated by Lafourcade, J Fouquet and Nativelli (Bull Soc franç de dermat et syph 36:1080 (Nov) 1929) They found, however, that in only 5 out of 23 cases did it occur in patients under *arsenobenzol* treatment, the remaining 18 being patients who were receiving *mercurial* or *bismuth* treatment, and who had not had *novarsenobenzol* for 2 or 3 months. The authors remark that it may be objected that since the majority of these patients had had *novarsenobenzol* previously, the jaundice was due to a delayed toxic effect; however, of the 13 cases under grey oil treatment, the jaundice disappeared after a further course of *novarsenobenzol*, and usually after the second or third injection. They conclude, therefore, that toxic icterus does not occur more frequently after arsenical treatment than after the administration of bismuth or mercury.

C Aubertin and R. Levy (Ann de méd 27:151 (Feb) 1930) state that it is now incontestable that blood disorders, particularly *agranulocytosis*, follow **antisyphilitic medication**, 28 cases having been collected from the literature. The sexes were about equally divided, contrasting thus with the predominance of females in Schultz's disease. The ages ranged from 11 to 50; the greater number, however, occurred between 20 and 40, the period in which the most active specific treatment is employed. Most of the patients were robust and, apart from the syphilis, showed no pathological abnormality. The previous duration of the syphilitic infection varied; in some cases it was re-

cent but in others the hematological symptoms did not appear for many years after the initial chancre. The blood changes rarely occurred during the first series of treatments, but usually were observed in the second and third; if *arsenobenzol* was the drug employed, the provocative injection seemed to lie between the fourth and eighth, and in doses between 0.3 and 0.9 Gm. (5 to 14 grains). A few cases showed some previous signs of intolerance, such as vomiting and fever. The interval between the causal injection and the onset of the *agranulocytosis* varied greatly; usually it ranged between 1 and 8 days, but in some cases it was prolonged to 2 or 3 weeks. The apparent onset is frequently abrupt and marked by chills, fever, intense malaise, and dysphagia. It may be preceded by a prodromal phase of 1 or 2 weeks, in which there is lassitude with headache.

The *agranulocytic* syndromes may be classified in 3 groups, *ie*, uncomplicated, complicated, and abortive. The first group is uncommon and resembles Schultz's disease. It is marked by an infectious condition, sometimes associated with icterus, and accompanied by buccopharyngeal lesions of an ulceronecrotic type. The blood shows a very marked leukopenia, with a complete or almost complete disappearance of the granular elements, but with no notable anemia, no signs of a hemorrhagic diathesis, no diminution in the platelets, and no abnormal forms. The second group may be subdivided into cases in which a simple or hemorrhagic purpura is superimposed on the *agranulocytosis*, and those in which an acute anemia, thrombopenia, and hemorrhagic signs are present. In the abortive forms the absence of granular elements is not so marked, and a hypopolynucleosis rather



than an agranulocytosis exists. Short notes of cases of each type are given. The *prognosis* is grave and the disease usually terminates fatally, cure is rare, being more common in the abortive types. The chief drug which causes agranulocytosis is arsenobenzol with its derivatives (the benzol group is known to be particularly hemotoxic), but other arsenical salts and the bismuth salts are also causative agents.

Attention is called by L. A. Cordivola and A. J. Guiray (*Semana med* 2 1279 (Oct 23) 1930) to the possibility of an *arterial embolism* after an intramuscular injection of bismuth (either soluble or insoluble salts of bismuth) in the treatment of syphilis. In order to avoid such a danger, the authors advise *sub-aponeurotic injections*. After the needle has been introduced, the entrance of blood should be expected, and a movement of slight aspiration should be made with the syringe before injecting its contents, in the event that the needle is obstructed, thus preventing the flow of blood. The injections should be made at the internal part of the buttocks where the blood-vessels are fewer than in some other parts of the buttocks. If arterial embolism is produced, it should be treated as soon as it is diagnosed.

The *symptoms* produced by arterial embolism are spectacular. The authors report a case in a syphilitic patient, aged 20, who immediately after the eighth intramuscular injection of bismuth had a painful reaction by the development of a hard local inflammation, pain that radiated to the entire leg, and the appearance of arborizations of dark red hue in the area in which the injection had been made, some of which arborizations ended in the formation of superficial scars. All symptoms proved to be caused by the presence of an arterial em-

bolism. The authors explain the mechanism which, in their opinion, is involved in the production of arterial embolism, and they present pictures of the observations made in the microscopic study of serial sections made after a biopsy.

Among 484 syphilitic patients who were given bismuth therapy, M. Taralrud (*Med Klin* 27 320 (Feb 27) 1931) noted *stomatitis* in only 9 cases and in all these patients the mouth hygiene was unsatisfactory. However, *renal disorders* developed in 57 per cent. The author concludes that, by correct dosage and by good care, inflammation of the oral mucous membrane can be prevented. More consideration should be given to the toxic disorders of the kidneys, which develop in the course of bismuth therapy and are generally of a type of tubular nephropathy. Their *prognosis* is generally favorable, especially if control tests of the urine are made regularly, and if the bismuth cure is interrupted as soon as pathological signs appear. However, it was also found that when the bismuth therapy was resumed, the renal disorder recurred. This contradicts Heimann-Trosien's statement that the kidneys become accustomed to bismuth. The author advises that before each bismuth injection, the mouth of the patient should be carefully inspected and albumin and sediment controls of the urine should be made. If bismuth therapy is discontinued on the appearance of the first pathologic signs, stomatitis as well as serious renal disorders can be avoided.

**CONGENITAL SYPHILIS.—TRANSMISSION.**—E. Martin and Vierkotten (*Monatschr. f. Geburtsh. u. Gynak.* 34:128 (Feb.) 1930) state that syphilis in the father can be transmitted to the child only through the mother;

the transmission always occurs by passage of the spirochetes through diseased villi in the placenta. Abortions up to the fourth month are not to be ascribed to syphilis. Characteristic of syphilitic infection are the macerated fetuses of the seventh and eighth months. The ratio between the weight of the placenta and that of the child is significant. In the newborn, the Wassermann reaction is uncertain during the first 6 weeks, it may even be negative in the presence of positive clinical symptoms. Children of mothers who have received thorough treatment previous to becoming pregnant should be given the same treatment as children whose mothers had a positive reaction during pregnancy.

In the fight against congenital syphilis, it is most important to recognize syphilis in the pregnant woman. Therefore, a Wassermann test should be made in every case of pregnancy. The pregnant woman is to be regarded as syphilitic if in 2 blood tests made at least 10 days apart the reaction is positive. Such women should be treated energetically with **neosalvarsan** and **bismuth**. The authors give 3 injections of 0.45 Gm (7 grains) of neosalvarsan within 14 days and repeat this treatment after an interval of 5 or 6 weeks. If the duration of the pregnancy will not permit repetition of the injections according to schedule, the interval may be shortened without harmful results. After delivery, the treatment is continued. Unmarried mothers and their children are kept at the Clinic until the treatment is completed.

The diagnosis of congenital syphilis in the child is based chiefly on the blood test of the mother, as clinical signs of the disease are usually absent in the infant. The diagnosis is confirmed when the spirochete is found in the um-

bilical cord (tissue fluids, frozen sections). The presence of osteochondritis and periostitis is easily determined by examination with the x-rays. The ratio between the weight of the child and the placenta is another aid in the diagnosis.

With regard to the *treatment of the child*, there is a difference of opinion. Gammeltoft (Denmark) is opposed to treatment when the serological reaction is not positive and there are no clinical signs of the disease. He emphasizes, however, that the child should be kept under observation for at least 6 months. As conditions are different in Germany, the authors demand that all "endangered" infants be given thorough treatment immediately after birth. "Endangered" children are those whose mothers were syphilitic before or during the pregnancy. These children should be reported to the clinics which have been established to give advice to mothers. In the Martin and Vierkotter's cases the "preventive" treatment of the newborn is begun on the third day after birth with **spirocid** tablets of 0.25 Gm (4 grains). The authors base their opinion on their experience with 117 babies. In the cases of prematurely born infants, they begin the treatment on the third day with one-fourth tablet. The treatment should be instituted gradually, but the dose increased as rapidly as possible until 1 tablet is given daily. If diarrhea or vomiting supervenes, the treatment should be stopped and after cessation of the symptoms should be begun again with the initial dose. The authors have observed cases in which the baby was able to tolerate 1 Gm (15 grains) of **spirocid** on the seventh day. The rapidity with which the dose can be increased depends upon the individual in-

fant No general rule can be laid down. The spirocid tablets are dissolved in mother's milk. For the entire treatment 30 Gm (1 ounce) of spirocid are used. Under this management the infants progress remarkably well.

The influence of hereditary syphilis of the progenitors on the product of conception is discussed by H. Paucot (*Rev. franç. de gynéc. et d'obst.* 25: 593 (Oct.) 1930). He distinguishes 2 types of hereditary syphilis, *i.e.*, the virulent and the dystrophic, one the result of the action of the toxin. However, the limits between them can only be artificial, since for the development of a dystrophy there must be virulent activity at some time.

The author investigated the function of reproduction in heredosyphilitics by studying families in which the mother, the father, or both parents had inherited syphilis. The majority belonged to the first group. The reproductive activity of 5 heredosyphilitic women, none of whom had fewer than 9 pregnancies, is shown in tables. Abortions were numerous. Sometimes the reproductive career began with a series of miscarriages; sometimes a series of miscarriages followed numerous full-time pregnancies, and sometimes full-time pregnancies and miscarriages were alternated. The whole series of obstetrical stigmata of acquired syphilis were present: hydramnios, congenital malformations, monstrosities, twinning, voluminous placentæ, and small atrophic placentæ. Most of the women were young and of good physical appearance, but some were disfigured. One presented thyroid hypertrophy, exophthalmia, typical dental changes, and positive Hecht and Desmoulières reactions. Her children were very delicate and only 2 survived. This case and 2

others demonstrate that there is no parallelism between the stigmata of inherited syphilis and the severity with which the product of conception is affected. The prognosis in a given case cannot be determined, but the incidence of fatalities (abortion, still-born infants, and early deaths) among the descendants can be forecast. In statistics published by the author in 1928 the mortality was 57 per cent. Hereditary syphilis is more often fatal to the descendants than acquired syphilis.

The cases of 2 women with a heredosyphilitic husband are summarized in the tables. These women had 4 abortions in 15 conceptions. Prematurity and the presence of stigmata and clinical signs were no less frequent than in the cases of maternal heredosyphilis. Twice the Wassermann reaction was positive. It may be concluded that hereditary syphilis is transmitted through the father to the second generation. The heredosyphilitic father may be vigorous and appear to be healthy.

When both parents have hereditary syphilis the results are disastrous. Fruhinsholz reported cases in which there were only 4 living children from 14 pregnancies. In the first case studied by Paucot there were 2 successive abortions and a macerated still-born fetus. The marriage of cousins brought out unmistakable signs of syphilis which had been almost extinguished in the second generation. Paucot states that the biological reaction set up by pregnancy is more sensitive than any of the humoral reactions.

The results of treatment of the mother during pregnancy are very encouraging. The mortality is decreased at least 6 per cent. It is necessary to resume treatment with each new pregnancy, as abortions and still-births occur

after pregnancies carried to term by the use of arsenicals and bismuth

The author believes that the spirochete passes through a larval form, that of an ultravirus which escapes detection by methods of examination now available. While experimental proof is lacking, clinical facts and serological findings do not disprove this hypothesis

**CONGENITAL SYPHILIS AND PUERPERIUM.**—The influence of congenital syphilis on pregnancy, delivery, the puerperium and later fate of children was studied in 39 mothers with established congenital syphilis, and 55 pregnancies by H Boas and T Sode-mann (Hospitalltid 72 1067 (Nov. 7) 1929), who found no evidence of increased danger to mother or child in pregnancy and delivery. Albuminuria of pregnancy occurred more frequently but was always mild, transitory and, as a rule, nonrecurrent. Of the 37 children observed for from 4 months to 17 years, all were clinically and serologically without syphilis; necropsy in 4 infants showed no signs of syphilis; 2 cases were abortions; in 13 children not examined afterward there were no signs of syphilis at birth. In spite of these results, intensive treatment during pregnancy, especially with arsphenamine, is advised for every patient with congenital syphilis

**PATHOLOGY.**—C. J. Watson (Arch Path 8:224 (Aug) 1929) reports the histologic appearance of the spleen in 4 cases of congenital syphilis, 3 of which presented severe anemia during life. The endothelial cells lining the sinusoids, as well as the macrophages free in their lumina, contained both nucleated and mature red blood cells, in addition to large amounts of hemosiderin. Normoblasts were of frequent occurrence, but there were no other signs

of myeloid metaplasia. In 2 cases examined the anemia was of a regenerative type, while in 1 the presence of bilirubinemia was associated with an indirect van den Bergh reaction. The author believes that these observations, together with the histologic changes in the spleen, constitute evidence that the anemias were hemolytic and imply that the spleen plays an important rôle in their origin

H H Perlman and C S Wright (Am J Syph 15 449 (Oct) 1931) present the result of a study that was instituted for the purpose of accurately determining the value of complete blood counts (red blood cell, white blood cell and differential counts) in the diagnosis or prognosis of congenital syphilis, and the effect of therapy on the *blood picture*. Although the actual number of cases studied was small, the authors believe that the study has particular value in that all the blood examinations were made by the same technician, a technician highly specialized in this type of work, thus eliminating all sources of error. As a result of the studies, they are forced to conclude that the secondary anemia may be *no more and no different* from that found in supposedly healthy children. No reliance can be placed on the degree of anemia as a diagnostic sign, nor does the study of the individual cells reveal anything of diagnostic or of prognostic importance. However, no cases of true syphilitic anemia were encountered in the study. Treatment with compounds of arsenic or bismuth, or with a combination of these 2 drugs, had a variable and inconsistent effect on the secondary anemia when present and on the differential count. This is in contrast with previously reported studies on the effect of mercury, which is a hemolytic agent, al-

though, paradoxically, mercury may cause an increase in hemoglobin in a patient with true syphilitic anemia.

From an interesting and somewhat unusual investigation bearing on the tooth pulp and maxillary bone in congenital syphilis, W. Bauer (Wien klin Wchnschr 44 879 (July 3) 1931) points out that the significance of *Hutchinson's teeth* as a sign of congenital syphilis is still being disputed, and he thinks that only microscopic examination of the tooth pulp and its surroundings in children with congenital syphilis who have not undergone treatment can reveal the effects of syphilis on the teeth. He reports the result of his microscopic investigations on the upper and lower *maxillæ* of a still-born infant and of 3 infants aged  $2\frac{1}{2}$ , 6 and  $6\frac{1}{2}$  weeks, respectively. All of these showed syphilitic symptoms such as syphilitic osteochondritis, gummas, syphilitic pemphigus and papules in the mouth. The results of the microscopic studies are summed up as follows: (1) In congenital syphilis spirochetes are demonstrable in the tooth germ, in the pulp of the noncalcified dentin, in the calcified dentin, in the dental sac, in the enamel germ and in the enamel epithelium. (2) The spirochetes are especially numerous in the areas of most intense growth, *i.e.*, the basal portion of the tooth germ. (3) The syphilitic process and the resulting vascular involvement and local circulatory disturbances cause changes of the odontoblasts, the ameloblasts and the dental sac. The hypoplasia of the enamel is probably the result of the injury of the ameloblasts, which, in turn, is caused by edema and hemorrhages. (4) The changes of the maxillary bones in congenital syphilis are a rarefying and fibrous inflammation of the bone-marrow and an ossifying periostitis.

**SYMPTOMS.**—G. K. Hgoumenakis (Deutsche Ztschr f Nervenhe 114: 288 (Sept.) 1930) calls attention to a sign of congenital syphilis which, he says, he had first described. The sign, which consists in *enlargement of the sternal end of the clavicle*, was frequently found among the 1500 patients examined. 23 of the most characteristic cases being reported. In all instances, besides this sign, other signs of congenital syphilis were present; in 7 instances, the Wassermann reaction was positive. The sign was never observed in healthy persons or in patients with an acquired syphilis. X-rays indicated that there was not an abnormal attitude of the patient or a distended bursa of the sternoclavicular joint, but an exostosis of the internal end of the clavicle. The development of the exostosis is explained by anatomic, biologic and mechanical factors. It is known that the sternal end of the clavicle first consists of connective tissue, which is early transformed into bone tissue. The syphilitic spirochetes carried by the blood become as readily localized in the connective tissue as in the lymphatic spaces and in the organs of the fetus. Later, as the result of the frequent movements of the arm and of the consecutive friction of the clavicle against the sternum, an activation of the spirochetes occurs. Their toxins cause an irritation, resulting in the appearance of a chronic periostitis and of an exostosis in the sternal end of the clavicle. In 13 cases in which the patients were left-handed, the enlargement was situated on the left clavicle.

**DIAGNOSIS.**—D. Nabarro (Brit. J. Ven. Dis 7: 1 (Jan.) 1931) discusses certain symptoms common in congenital syphilis, the nonrecognition of which leads to diagnostic errors. Frequently a

child is born apparently healthy, but it develops snuffles and, some weeks later, a rash, which must be differentiated from the napkin rash due to irritation by urine, the latter rash is usually brighter and less extensive. Condylomata, not common in children, are rarely seen before the age of 1 year, these lesions are usually characteristic. Syphilitic osteoperiostitis or epiphysitis are demonstrable by systematic x-ray examinations. A mild hydrocephalus may be associated with inherited syphilis in early childhood. An important symptom of neurosyphilis, often overlooked, is inequality of the pupils with or without reaction to light and accommodation.

Spastic paraplegia is another overlooked symptom, this may be a monoplegia, diplegia, or paraplegia. Bilateral hydrarthrosis, especially of the knee, is usually of a syphilitic nature. Interstitial keratitis is the commonest symptom of late inherited syphilis. Minor degrees of Hutchinsonian teeth often occur. Nabarro emphasizes the importance of the Wassermann test in all doubtful cases, and the need of its repetition if the reaction is doubtful. He believes that **mercury** alone is not a reliable drug in congenital syphilis, but that it should be associated with an **arsenical**; as soon as the diagnosis is made he begins injections of some **arsenical** or **bismuth** preparation. In certain cases it is advisable to start with mercury for a few weeks and then to give very small arsenical injections.

A new clinical guide is suggested by A. G. Alarcon (Arch d méd. d enf. 32 589 (Oct) 1929) in the diagnosis of syphilis on the basis of a typical intestinal disorder occurring in children under 3 months of age. He calls this the transitional dyspepsia of infants. It is characterized by symptoms occurring

during the first days of breast feeding. Shortly after feeding, regurgitation and hiccough occur, which at times may awaken the infant. The intestinal disorder is evidenced by crying. Vomiting is rare in breast-fed infants, although frequent in artificial feeding. Acid diarrhea with erythema of the buttocks follows the initial constipation. The author divides the condition into a preliminary stage lasting 3 weeks, a secondary stage lasting 6 weeks and a final stage lasting 3 weeks, and he feels that the influence of syphilitic septicemia on the nervous system is the most frequent cause. The early onset, with the exaggerated symptoms and the prolonged duration, are suggestive of the underlying lues.

The *Wassermann test* and color reactions are believed by F. W. Gregor (Arch Dermat and Syph. 24 733 (Nov) 1931) to be of distinctive service in inherited syphilis, whereas tests for albumin and cell counts are valuable only after other infections have been ruled out.

The *enzyme reaction* was found by U. de Gironcoli (Pediatria 37 1260 (Nov 15) 1929) to be more sensitive than the Wassermann test, especially in treated cases of syphilis and in cases in which the personal history pointed to syphilis. While the enzyme reaction need not entirely replace the Wassermann test, it should be, in every case, the necessary complement by reason both of the results that it gives and of the simplicity of the technic.

H. Schonfeld (Jahrb. Kinderh 129 335 (Nov) 1930) reports a case of multiple foci of degeneration in the diaphysis of the long bones of an infant with congenital syphilis. Because of band-shaped shadows of great density and approximately parallel to the epiphyseal



lines, he believes that the foci of degeneration in the diaphysis of the bones were not the result of primary osteitic or osteomyelitic syphilitic processes but of osteochondritis.

#### DIFFERENTIAL DIAGNOSIS.

—The problem of early genital lesions is considered by O C Wenger, A A Surgeon, and H O Proske (Am J Syph 14 313 (July) 1930) who state that their experience has proved that the differential diagnosis of the two lesions (chancre and chancroid) is possible by repeated examinations and careful observations in 86 per cent of the cases studied. In the remaining 14 per cent. of this series, the diagnosis remains in doubt, because all of the patients were transient, not being sufficiently intelligent to realize the importance of the 6 months' period of observation. The authors believe that the general practitioner would be justified, from the standpoint of public health, to regard all early genital lesions as probably chancre where he has no proper facilities for making a differential diagnosis, since the criterion for the diagnosis of chancroid is impracticable except in a few cases. Only in very rare instances, and where the patient is under perfect control, should the physician wait for possible later manifestations of syphilis, since they are always uncertain. If all cases of early penile lesions were treated as early syphilis, many new infections and a great deal of latent syphilis would be prevented.

On the basis of his observations in 50 cases of congenital syphilis, N Asherson (J. Laryng and Otol 46:326 (May) 1930) concludes that the "*compression nystagmus*" sign is a not uncommon concomitant in patients with congenital syphilis who have received extended treatment. A characteristic

lead blue tympanic membrane is described. The infrequency of chronic otorrhea and the incidence of deafness in cases of congenital syphilis is commented on.

Nine cases of *rheumatic infection* in congenital syphilitic children are described by A D Fordyce (Brit M J 1 530 (Mar 22) 1930). In 6 of the cases there were no obvious signs of congenital syphilis. It is suggested that undetected syphilis may in some cases form a basis for the serious course of rheumatic infection, and, further, that the study of rheumatism may be aided by the grouping of rheumatic cases along nonrheumatic lines.

A case of pseudosyphilis of *external genitalia* was reported by J Gay Prieto (Arch españ de pediat 14:705 (Dec) 1930) in a patient aged 7 months (a daughter of a syphilitic patient previously treated and whose serologic reaction became negative for syphilis) who presented an apparently syphilitic lesion of the vulva. Ultramicroscopic examination of the exudate from the papules and the examination of the patient's blood gave negative results for syphilis. The good results obtained with a treatment which consisted of an indifferent paste and methenamine confirmed the nonsyphilitic etiology of the exanthem in this case. The characteristics of several kinds of exanthems resembling syphilis which appear on the external genitalia in female infants are reviewed in relation to the differential diagnosis with the author's case. Especial reference is made to certain forms of lesions, such as simple forms of syphiloid dermatitis, chancriform pyodermitis, pseudosyphilis of the external genitalia (similar to that type which Lipschutz described in adult women with vaginal discharge) and lichen ob-

tusus Owing to the aspect of the patient's lesions and to the presence of vulvitis, the author's case should be considered as pseudosyphilis of the Lipschutz type in spite of the scanty lesions in the gluteal region similar to a form of papulous infantile erythema. The author reaches the following conclusions: There is in female infants a form of condylomatous pseudosyphilis clinically similar to pseudosyphilis of the Lipschutz type. The clinical symptoms and the presence of syphilitic lesions on the external genitalia of female infants should not form the basis of a diagnosis of syphilis unless the serologic tests and ultramicroscopic examination of the lesions confirm the clinical diagnosis. Otherwise, the aspect of the lesions may lead to error in the diagnosis.

**TREATMENT.**—J. F. Coppolino (Am J Dis Child 39:288 (Feb) 1930) used bismuth salicylate in oil suspended with camphor and creosote, 1 c.c. (16 minims) of which contained 130 mgm. (2 grains) of metallic bismuth in the treatment of congenital syphilis. In the earlier cases he started with a dose of from 15 to 30 mgm. ( $\frac{1}{4}$  to  $\frac{1}{2}$  grain) in young infants, and 65 mgm. (1 grain) in older children. It was observed that no ill effects followed, and the dose was increased to 65 mgm. (1 grain) for children under 1 year of age, and to 130 mgm. (2 grains) in older children. The course of treatment consisted of 20 injections at weekly intervals. A blood test was taken at the beginning and termination of each course and if it was positive, the treatment was immediately continued, if negative, a 4 weeks' rest was allowed. The maximum number of courses administered was 3, after which the patients returned every month for examination and blood tests. Twenty-six children

were treated. Bismuth in rather large doses is apparently well tolerated by infants and children. It is useful in the treatment of older children but does not effect a cure. It is most efficacious in young infants, rendering them both symptom-free and serologically negative, but Coppolino does not feel that any absolute evaluation of the drug can be made at the present time.

**Inoculation Malaria.**—G. Ahman (Hygea 91:673 (Oct 15) 1929) made 40 inoculations in 36 cases, mostly refractory and unfavorable in prognosis. The results seem to him to encourage continued attempts on a larger scale.

**NEUROSYPHILIS.—ETIOLOGY.**—The theory that hereditary nervous syphilis is due to a neurotropic virus distinct from the dermatropic virus of syphilis is not accepted by A. Sézary (Bull et mém Soc med d hôp de Paris 54:1182 (July 7) 1930). He cites the cases of a family in which the virus attacked the nervous system of the parents and of one child, sparing the nervous system of the second child, but attacking the bones of the nose. The same virus was therefore neurotropic and osteotropic, which proves that it has no definite organotropism.

**SYMPTOMS.**—J. J. Minz (Sovrem psikhonevrol. 11:300 (Oct-Nov) 1930) reports 4 cases of *cerebellopontile angle syndrome* in syphilis of the central nervous system. In all of the cases there was noted involvement of the fifth, seventh and eighth cranial nerves (which originate at this angle), cerebral manifestations of various degrees and general brain symptoms (headaches, vomiting). There also have been observed some remote effects, as paresis of the abducens, of the ninth and tenth, or of the ninth and twelfth nerves. Besides cranial nerve involvement there

were also symptoms due to pressure on the pyramids (increased reflexes) on the opposite side. As a sequel to the intracranial pressure, eye symptoms developed, *i e*, neuroretinitis, neuritis, and atrophy of the optic nerve. The women patients complained of amenorrhea of 4 to 5 months' duration. The Wassermann reaction of the blood and cerebrospinal fluid was positive in all cases.

From a review of the literature, the author concludes that the cerebello-pontile angle syndrome in syphilitic involvement of the central nervous system is not rare. In some instances this symptom complex occurs in an almost pure form; in others it is combined with other symptoms. The great practical importance of its early recognition should be emphasized. With the employment of serologic methods of investigation this is easy on account of the combination of cerebrospinal phenomena. In cases in which the diagnosis is difficult, antisyphilitic therapy should be used, under which the patient improves rapidly.

An unusual case of *cerebral syphilis* in a girl, aged 9, who suffered from hemiplegia and aphasia, is reported by G. Papp (Wien klin. Wchnschr 42: 1503 (Nov. 21) 1929). The child had been apparently healthy until the day before she was brought to the hospital when she had complained of feeling weak and tired. After she had slept for several hours, she could not speak and showed signs of a beginning paralysis. Because the symptoms became more severe, the child was sent to a hospital. The author gives a detailed report of the results of the examination. He states that the Wassermann reaction of the blood and of the cerebrospinal fluid was strongly positive. Under the influence of antisyphilitic treatment, the

paralysis gradually decreased. Because the patient contracted diphtheria, the antisyphilitic cure was interrupted but later it was resumed. However, the Wassermann reaction remained positive. It could not be definitely determined whether this was a case of congenital or acquired syphilis. Most of the characteristic signs of congenital syphilis were absent and the mentality of the girl was normal. After the birth of the child such symptoms as vesicles, sores and eczema had not been noticed. The mother had had no abortions and another child, 3 years older than the patient, was entirely healthy. This child, as well as the father, gave negative Wassermann reactions, whereas the reaction in the mother was strongly positive. The author believes that by means of prolonged treatment, it might be possible to counteract the syphilis. However, he questions whether the spastic hemiplegia will ever completely disappear.

**COMPLICATION.**—*Subarachnoid hemorrhage* complicating neurosyphilis is a clinical entity probably caused by rupture of diseased pial capillaries or vessels, according to I. J. Sands (Arch. Neurol. and Psychiat 24:85 (July) 1930). The underlying pathologic process is syphilitic meningitis, demonstrated by thickened leptomeninges, infiltration with lymphocytes and plasma cells, marked endarteritis of the fine capillaries of the pia, and hemorrhage in the subarachnoid space. The brain tissue proper shows marked glial reaction and syphilitic endarteritic processes in the capillaries. The clinical picture presented is that of subarachnoid hemorrhage plus the presence of positive serologic tests.

**PROGNOSIS.**—Discussing the great progress of syphilology for 2 de-

cludes and mentioning the optimistic conclusions the modern physician has made in regard to the diagnosis and therapy of syphilis, M Astvatzaturoff (Vrach Gaz 35 165 (Feb 15) 1931) shows the necessity of revision of this optimism concerning neurosyphilis. He puts foremost 3 points (1) Is it possible to make in a syphilitic patient, on a serologic basis, any prediction with regard to development of neurosyphilis in the future? (2) Is it possible to prevent neurosyphilis with arsphenamine therapy? (3) Should neurosyphilis be treated by arsphenamine? These questions are at present of great importance. The author emphasizes that the Wassermann reaction is nonspecific for syphilis not only biologically but also practically, *i e*, as was proven long ago, it could be positive in various other diseases (malaria, leprosy and scarlet fever). On the other hand, it can be negative when syphilis is present clinically. Many patients have been observed in whom neurosyphilis developed while their Wassermann reaction was negative for years. Therefore, a negative Wassermann reaction is not at all a guaranty that the individual will not be affected with neurosyphilis in the future.

To avoid the gross mistake which so many practitioners are making in pronouncing their patients cured, the author stresses the supremacy of the clinical signs over all others. The practitioner should be guided only by them in making his prognosis on neurosyphilis in the future. Also, in establishing a suitable syphilis therapy, serologic reactions are not of much value. Science has not yet developed means by which the possibility of neurosyphilis developing in a patient with a history of syphilitic infection can positively be excluded.

In regard to his second question, Astvatzaturoff states that antisyphilitic therapy in general and arsphenamine therapy in particular are unable either to prevent or to postpone neurosyphilis. As to the recent complaints in the special literature on some unfavorable by-effects of arsphenamine therapy, the author brings out that, although he has done extensive work in this direction, he has not yet come to any definite conclusions. But the statistical investigations on tabes made on quite a large scale by a collaborator demonstrate that the incubation period in patients treated with arsphenamine was much shorter (7 years) than in those who have not been under arsphenamine therapy (12) or who have been given treatments with mercury (14). All observations mentioned indicate that there is no use to talk about arsphenamine therapy as the specific or preventive treatment for neurosyphilis.

His third problem is closely related to the subject of the nature of neurosyphilitic phenomena. There is no doubt as to their ultimate connection, it is only not quite clear what is the nature of such a connection of the pathogenic relationship between syphilis and neurosyphilis. All recent efforts to cure neurosyphilitic phenomena with arsphenamine have been unsatisfactory. The new way of approaching it lies not in the sphere of antisyphilitic medications, but in "nonspecific" therapy (malaria).

The unfavorable by-effects of arsphenamine therapy in the treatment of neurosyphilis (encephalitis, "neuroretardives") which are not peculiar to other antisyphilitic agents, force the practitioner not only to withhold their use in the treatment of neurosyphilis, but to avoid them in many purely syph-

ilitic conditions of the nervous system, as the latter ones are easily treated with mercury and the iodides.

The author summarizes his conclusions as follows: (1) All serologic, cytologic, and chemical methods of diagnosis of syphilis and neurosyphilis must be taken into consideration only in connection with the clinical examination. (2) The negative results of the laboratory examinations cannot serve as a sign of a complete cure and do not exclude the possibility of neurosyphilis in the future. (3) As there are no methods of diagnosis which will completely eliminate the possibility of neurosyphilis in the future and there are not developed yet means for its preventive treatment, the practitioner never has the right to pronounce the patient completely cured. (4) With the modern methods of syphilis therapy neurosyphilis cannot be prevented or cured.

#### TREATMENT.—*Arsphenamine*.

—The antisyphilitic treatment of the central nervous system is discussed by H. H. Reese (J. A. M. A. 94: 455 (Feb. 15) 1930), who states that it is not known whether the antisyphilitic agents are spirocheticidal or the body resistance becomes increased and the activity of the spirochetes reduced. The type of therapy should be outlined for each individual case, with substitution of the drug of choice if it is not successful after a certain period of time.

**Intraspinal treatment** is the one of choice in cases of rapidly advancing meningeal involvement, with severe crises, optic atrophy and increased intracranial pressure, and in those cases which present an intolerance to intravenous injections of *arsphenamine*.

Primary and secondary syphilis should be treated with arsenicals if the spinal meninges are more or less acutely in-

flamed. 1.55 mg (1/120 to 1/60 grain) of **neoarsphenamine** (1/120 to 1/60 grain) may be given subcutaneously a week, according to Herberich. If the fluid is metastasizing, change to even more than from 0.3 to 0.5 mg (1/200 to 1/120 grain) should be given in from 40 to 60 cc (1 1/2 to 2 ounces) of spinal fluid at intervals of 3 weeks. If a tabetic patient does not react subjectively and clinically to 0.3 or 0.5 mg (1/200 to 1/120 grain) intraspinally, the neoarsphenamine medication may be increased to 0.75 and 1 mg (1/60 to 1/45 grain). To relieve subacute symptoms referable to a basilar meningitis, neoarsphenamine can be given intraspinally by the cisternal route in doses of from 0.5 to 1 or 1.5 mg (1/120 to 1/60 or 1/45 grain) or by a double puncture in the lumbar regions where the liquor in the lower buret pushes the liquor containing 0.5 to 1 mg (1/120 to 1/60 grain) of neoarsphenamine in the upper buret brainward. Both administrations endeavor to keep the neoarsphenamine in the basilar cistern and necessitate rest in bed for at least 36 hours with the patient in the Trendelenburg position.

**Arsphenamine** is the most stable arsenical with uniform toxicity and the greatest therapeutic effect, and is superior to neoarsphenamine. The inconvenience of its preparation and administration and the exigencies of office practice have led to the substitution of other arsenical preparations. The single dose should never exceed 0.6 Gm (10 grains) and it should be given only once a week. Advanced cardiovascular disease is a contraindication to its use. **Neoarsphenamine** has a somewhat lower therapeutic efficiency than *arsphenamine* and necessitates a larger number of injections. It has a marked tonic effect, produces less gastrointes-

tinal reaction and is less irritative to the veins. Because of its much simpler administration, its use is more widespread, at least in office practice.

*Disadvantages* of arsphenamine and neoarsphenamine are the anaphylactoid or nitritoid crises, but preventive drugs such as atropine, epinephrin and ephedrine are able to check these unpleasant occurrences.

Silver arsphenamine is said to be from 2 to 3 times as effective a spirocheticide as arsphenamine, but clinical experience has proven that it is not superior to other arsenicals. **Sulpharsphenamine** is the arsenical preparation of choice where intravenous medication is difficult or impossible. It is  $2\frac{1}{2}$  times less active than neoarsphenamine therapeutically and doses of from 0.4 to 0.6 Gm (6 to 10 grains) are given intramuscularly at weekly intervals. **Tryparsamide** is superior to all other forms of intravenous arsenical treatment in neurosyphilis. Generally the dose is 3 Gm. (45 grains) per injection, but individual case adjustment necessitates variable doses of from 2 to 5 Gm. ( $\frac{1}{2}$  to  $1\frac{1}{4}$  drams) with a considerable latitude as to the intervals during its administration. As a rule, the patients should be prepared, especially those with tabes, with **mercury inunctions** or weekly intramuscular injections of from 0.05 to 0.1 Gm. ( $\frac{3}{4}$  to  $1\frac{1}{2}$  grains) of the salicylate in a palmitin base and **potassium iodide** from 3 to 10 minims (0.18 to 0.6 c c) 3 times daily for 4 to 6 weeks before arsenical medication.

The parenchymatous cases should be treated by nonspecific methods, among which **malaria** is most efficient.

**Nonspecific and Malarial Therapy.**—The therapy of *paresis* is reviewed by H. H. Reese (Am. J. Syph. 13:348

(July) 1929) and he mentions particularly the use of **tuberculin**, **vaccine therapy** and the use of nonspecific agents, *ie*, **peptone**, **milk**, **turpentine**, **aolan**, and **sodium nucleinate**. Including the more recent reports in the therapeutic use of **intermittent fever** and **rat-bite fever**, the author believes that the best results are obtained with **malarial therapy**, particularly when supplemented by **tryparsamide**, **mercury** and **iodides**. Reese uses 6 to 10 c c ( $1\frac{1}{2}$  to  $2\frac{1}{2}$  drams) of infectious blood by intravenous inoculation for the average patient. Reinoculations after 8 to 15 months are most successful when the infectious blood is introduced intramuscularly as well as intravenously. Determination of blood groups in donor and recipient is advisable. After the patient has had from 3 to 6 chills, the author routinely uses such cardiac stimulants as **camphorated oil** or **caffeine**. **Digitalis** is avoided because of the bradycardia it may induce in conjunction with the later quinine. Modifying the severity of the general reaction, small doses of **quinine** are given. This procedure, it is hoped, will have a tendency to lessen the mortality rate. *Indications for interruption of the malarial infection* are poor physical condition, intercurrent disease, jaundice, nasal or oral hemorrhages and an increase of the blood urea (O'Leary's urea-nitrogen index). Organic metabolic diseases, circulatory diseases with high systolic and low diastolic pressure and chronic alcoholism are *contraindications to malarial therapy*. Aortitis or myocarditis without decompensation is not always a contraindication.

Reese comments on the complexities of the factors operating in malaria therapy. A disturbance of the vegetative reflexes results in the emigration



of the leukocytes toward the seat of an inflammation, and the author visualizes a similar activity in and about the inflammation of the nervous system. If the effect obtained in paresis is due to increased omniscellular activity, such a hyperactivity is the result of altered vasomotor equilibrium accompanying or following the malarial chill, and not the result of fever or some questionable antibodies. The chills, by altering the vegetative balance of the vasomotor system, with resulting dermatographism, peripheral leukopenia and a drop in blood-pressure, produce renewed and intense activity in areas of chronic inflammation. The majority of the cases treated were paresis. The pathology in *tabes dorsalis* is so different from that of paresis that it would be difficult to see how malaria could possibly change tract degenerations and their clinical manifestations.

Improvement was obtained in 42 per cent of the men and 45 per cent of the women. Fair results were obtained in 23.8 per cent, and a mortality rate of 4.6 to 8.5 per cent was encountered.

Successful results in the therapy of paretics is defined as a restoration of mental capacity, the control of the emotional sphere and a good insight into ethics and law. The ability to resume a lucrative occupation is the best gauge of such results. The writer warns against the malarial remittent paretic, however, as one who often lacks quick and sound judgment and is apt to err suddenly, and, as such, is not fitted for positions of responsibility which might require these exactions.

The present status of neurosyphilitic patients who have had nonspecific treatment and who have been under observation for from 3 to 5 years is discussed by P. A. O'Leary and L. A. Brunsting

J. A. M. A. 44:452, Feb. 15, 1930.  
In 100 patients who had with *tabes dorsalis* during the period June, 1924, to June, 1926, early signs of *paresis* had been evident before the treatment was instituted. The majority had other treatments for neurosyphilis. Of this number, 38 are in full remission, 31 are improved, 17 have not been benefited, 14 are dead. Only those capable of supporting themselves and their families are classed as "in remission." Five of the deaths resulted from the malaria, 3 from *paresis*, the remaining 6 from other causes. In most cases of remission the serological reactions of blood and spinal fluid are negative.

In *tabes dorsalis* the results have been less satisfactory. Of 13 patients, 4 are in remission, 3 are somewhat improved, 6 are dead. These patients had been under treatment for *tabes dorsalis* for years but had grown progressively worse, and treatment by malaria was tried as a last resort. The authors regard cases of this type as unsatisfactory for fever therapy, as the progressive downhill course is frequently accelerated by the treatment.

A group classified as *paresis sine paresi*, as asymptomatic paresis, including a number who had failed to respond to intravenous, intramuscular and intraspinal measures, gave satisfactory response to fever therapy. In these cases there had been evidence of clinical progression and failing acuity, but not sufficient mental impairment to warrant a diagnosis of paresis. In this group of 22, 10 showed negative serological reactions and decided clinical improvement, 6 have improved, 4 have not benefited, 2 have died. Patients of the type included in this group are regarded by the authors as ideal cases for fever therapy.

Encouraging results are reported in the **malarial treatment** of *neurosyphilis associated with acute syphilis of the meningeal type*, but in *tabes dorsalis* the results have not been very satisfactory. In general the authors recommend fever therapy when prolonged treatment with the arsphenamines and mercury, commenced early, has failed to control unfavorable progress, as indicated by the condition of the spinal fluid. The serological reaction, however, is not always an index of the value of treatment. Clinical improvement is not necessarily paralleled by serological improvement, while negative serological reactions are sometimes obtained without clinical improvement.

The authors have used **typhoid vaccine**, intravenously, to reactivate the chills and fever of patients in whom the malaria aborted after a short and incomplete course. They have also used it in cases in which malaria could not be induced. As yet, they feel indisposed to pronounce judgment on its merits, but state that a larger series of large doses of the vaccine are needed to produce satisfactory reactions. In their experience thus far, remissions have been less frequent and less pronounced under the vaccine treatment than under malaria.

In a symposium on 5 years experience with the **malaria treatment** of neurosyphilis, M. A. Bahr (Indianapolis M. J. 33.731 (Dec) 1930) states that of 240 cases of *paresis*, 29 per cent have been discharged as "recovered," *i. e.*, they have been able to return to their former occupations, show a minimal degree of intellectual defect, and have complete insight into the nature of the disease. The great majority of patients are found to be well advanced in the second or even in the third stage of the disease on admission to the hospital,

but those selected for the treatment were chosen "more or less indiscriminately," so that much better results might be expected from treatment commenced in the incipient stage. The treatment is easily controlled, but should be restricted to hospitalized patients. The most satisfactory time to take blood for inoculation is just before the chill is expected. Inoculated malaria is very sensitive to quinine, and cannot be transmitted by flies or mosquitoes, so that the treatment is not attended with danger to the public.

F. Prenat (*Ibid* 33 733 (Dec) 1930) presents an analysis of the outcome of the first 100 cases treated (1925 to 1927), and compares the results with 100 cases treated by **tryparsamide** in the same period but at another hospital. Prenat reports 25 patients discharged as recovered, 4 fit to leave hospital if a favorable environment were to be found, 4 remaining in hospital where they are good workers, 24 unimproved, the others (43) are dead. The tryparsamide results are as follows: cured, 5, improved, 40 (15 have left hospital); unimproved, 34, dead 21.

The serological outcome of the first 100 cases is dealt with by A. M. de Armond (*Ibid* 33 735 (Dec) 1930), who reports improvement in this respect in the majority of cases. The serological improvement, when it occurs, follows clinical remission. Reduced cell count is the first improvement manifested. A completely negative globulin reaction is not the rule. The intensity of the gold curve is reduced by a gradual flattening. Two years or more elapse before the Wassermann reaction becomes negative.

C. P. Clark's contribution (*Ibid* 33 737 (Dec) 1930) is that of an ophthal-

mologist. In reporting his observations on 50 patients, he found that 6 with unilateral Argyll-Robertson pupils and 22 out of 28 with bilateral Argyll-Robertson pupils recovered normally pupillary reactions. This was the outstanding improvement. Clark suggests that **malaria-inoculation** would be of value in *syphilis of the optic nerve or visual pathways*.

The *mechanism of malaria treatment* is discussed by W. L. Bruetsch (*Ibid* 33 739 (Dec.) 1930). He disagrees with those who attribute the results obtained to the rise in temperature which follows inoculation. "During the malaria treatment specific tissue changes are going on in the body and it would be strange if those changes would not come into action in destroying spirochetes." His study of material from autopsies of patients who died while under the treatment revealed a stimulation of the reticulo-endothelial system leading to new formation of phagocytic tissue in all organs of the body, especially in the liver and spleen, where there is normally a large mass of reticulo-endothelial tissue. Histocytes are numerous, particularly in the venous blood of the liver, in the vessels of the mucosa and submucosa of the small intestines, and in the septal vessels of the lungs. They are present in great numbers in the meningeal veins and in lesser numbers in the cortical vessels. It is significant that new formation of macrophagic cells is found in the connective tissues everywhere throughout the body, as spirochetes are found in the connective tissues, and it is known that tissue phagocytes are capable of engulfing spirochetes. A similar, but less marked, stimulation of the reticulo-endothelial apparatus can be induced by typhoid vaccines and various proteins. Doubt-

less other factors are concerned, but of these no definite knowledge is yet available.

P. Romberg and J. Barly (Paris med 1 452 (May 17) 1930) discuss the objectionable features of malaria therapy in *infantia paralytica and tubes* and in its stead recommend inoculations with *Spirochæta hispanicum* variety *maroccanum*. The spirochete can be readily cultivated in guinea-pigs and the blood of the infected animals used for the inoculation of patients. The fact that the inoculations are not made with blood from another patient is of particular significance in cases in which the patient is being treated for some nonsyphilitic condition of the central nervous system, as multiple sclerosis, parkinsonism or dementia precox, because it eliminates the possibility of simultaneous transmission of syphilis. In order to produce an infection with *Spirochæta hispanicum* variety *maroccanum*, it is only necessary to place on the conjunctiva or in the nasal fossæ of the patient several drops of blood from an infected guinea-pig. The first febrile attack occurs from the sixth to the tenth day after inoculation. The subsequent attacks appear at regular intervals and their intensity should not be modified with injections of arsphenamine or acetarsone, because the greater their severity, the greater the therapeutic affect.

**SYPHILIS, CONGENITAL.—**  
**INCIDENCE.**—H. McCulloch (Am. Heart J 6 136 (Oct.) 1930) states that of 40,470 children under 15 years of age admitted to the St. Louis Children's Hospital during the 10-year period from 1915 to 1924 inclusive, 939 or 2.3 per cent. were found to have syphilis. Stokes, according to R. R. Sullivan (Minnesota Med 13 302 (May) 1930)

places the incidence of syphilis in the child population as ranging from 3 to 5 per cent. Sullivan concludes that congenital syphilis is more prevalent than is generally believed and is a definite clinical problem.

**ETIOLOGY.—Predisposing Cause.**—It is generally recognized that the nearer the time of infection of the female adult to the time of conception, the greater is the danger of syphilitic infection of the fetus. E. D. Osborne and E. D. Putnam (New York State J. Med. 31:18 (Jan. 1) 1930) point out that in view of the fact that 90 per cent of infections occur before the seventeenth and twenty-fifth year of life, which corresponds to the period of greatest reproductive activity, it is not surprising that 40 to 50 per cent of all pregnancies in syphilitic women result in miscarriages or still-births. On the other hand, the author emphasizes that although the time element is an attenuating factor, it cannot be relied upon and they note 3 instances in which women have been giving birth to syphilitic infants over a period of from 12 to 15 years.

**TIME OF INFECTION.**—The time during pregnancy in which infection is most likely to be transmitted to the fetus seems to be pretty well agreed upon, according to E. J. Trow (Canad. M. A. J. 23:48 (July) 1930). Many excellent observers have reasons for assuming that infection of the fetus usually does not occur before the fourth and fifth month of pregnancy and that it may occur much later.

**TRANSMISSION TO THIRD GENERATION.**—A. Deutsch (M. J. and Rec. 132:78 (July 16) 1930) reports what he considers an unquestionable instance of transmission of syphilis to the third generation. Syphilis in the

grandmother was transmitted to her children and by them to the grandchildren. D. M. Greig (Edinburg M. J. 37:349 (June) 1930) reports 4 somewhat similar cases which, he states, some future observer will probably incorrectly interpret as transmission of the disease to the third generation.

**MANIFESTATIONS.—Placenta.**—T. Brandt and K. Sieck (Acta obstet. et gynec. Scandinav. 8:431, 1929) determined the weight ratio of the newly born infant to the placenta to be 1:3.0 to 7:6. The ratio does not vary remarkably for the syphilitic infant. A relatively heavy placenta is a sign of prematurity and not of syphilis.

**Eye.**—Nystagmus, according to N. Asherson (Arch. Dis. Childhood 5:331 (Oct.) 1930), is not an uncommon concomitant of congenital syphilis among treated cases occurring in infancy and childhood.

J. S. Friedenwald (Bull. Johns Hopkins Hosp. 46:185 (Feb.) 1930) has given the following clinical classification of the pathological changes of the eye seen on ophthalmoscopic examination: (1) *Circumscribed chorioretinitis* with focal lesions, sometimes multiple in the choroid and retina, (2) salt and pepper *fundus*, occurring early in life and presumably the end-result of fetal or early infantile inflammation, (3) *retinal scarring* with atresia of the retinal blood-vessels and with optic atrophy, (4) *retinitis pigmentosa*, occurring (a) in infancy merely as an exaggeration of the "salt and pepper" process and (b) occurring in later life.

**Ear.**—In a group of 50 cases of congenital syphilis studied by N. Asherson (J. Laryng. and Otol. 46:326 (May) 1931), 4 were deaf. Asherson further observed that in 12 of the children the drum membrane, instead of being pearly

white in color, had a peculiar *steel blue* appearance. The author could find no evidence that chronic infection of the ear occurs more commonly in syphilitic than in normal children. Indeed, chronic otitis media is rare among children with congenital syphilis under treatment, in spite of the presence of a positive Wassermann reaction and other stigmata of the disease.

**Lip.**—G. Mestchersky (Urol and Cutan Rev. 34:27 (Jan.) 1930) reports 2 cases of congenital syphilis with a relatively new sign of congenital syphilis known as the "fissure of Milian." According to the author, the lesion which was first described by M. Milian in 1925, is characterized by a more or less deep, persistent fissure placed perpendicularly, especially in the lower lip. The lesion is painful, particularly in cold weather.

**Teeth.**—According to Mestchersky (*loc cit*), the absence of 1 or 2 *lateral incisors* may occur in congenital syphilis. W. Bauer (Wien. klin Wchnschr 44:879 (July 3) 1931) states that the significance of Hutchinson's teeth as a sign of congenital syphilis is still being disputed. He thinks that only microscopic examination of the tooth pulp and its surroundings in untreated children with congenital syphilis can reveal the effects of syphilis upon the teeth. The author examined the upper and lower maxillæ of 1 stillborn infant and 3 infants aged 3½, 6 and 6½ weeks, respectively. Spirochetes were demonstrated in the tooth germ, in the pulp in the noncalcified dentin, in the calcified dentin, in the dental sac, in the enamel germ and in the enamel epithelium. The spirochetes were especially numerous in the areas of most intense growth, *viz*, the basal portion of the tooth germ. The syphilitic process and the resulting vas-

cular involvement and local circulatory disturbances cause changes of the odontoblasts, the ameloblasts and the dental arch. The hypoplasia of the enamel is probably the result of the injury of the ameloblasts which, in turn, is caused by edema and hemorrhages. The changes of the maxillary bones in congenital syphilis are due to a rarefying and fibrous inflammation of the bone-marrow and an ossifying periostitis.

**Trachea.**—Involvement of the trachea without infection of the larynx apparently occurs but rarely. F. J. Collet (J. de méd de Lyon 10:451 (July 20) 1929) reports a case of this type occurring in a 9-year-old-girl with congenital syphilis. The symptoms were those of stenosis with a compression cough and paroxysmal dyspnea, but without change in the voice. The symptoms were relieved by antiluetic therapy.

**Lungs.**—E. Apert, L. Girard and Rappoport (Bull Soc de pédiat de Paris 27:174, 1929) report a case of *bilateral disseminated pulmonary emphysema* due to congenital syphilis. The authors concluded that asphyxia was caused by the enlarged tracheobronchial gland pressing upon the trachea. The very strong respiratory effort exerted by the weakened lungs, which were infiltrated throughout by gummatous lesions with an associated obliterating arteritis, was thought to have produced the unusual picture resembling emphysema.

A new sign of syphilis is described by F. Herb (M. J. and Rec. 132:74 (July 16) 1930), which he refers to as *pulmonary stigma*. According to the author, the condition is characterized by physical findings at the lower, posterior aspect of the right lung that indicate a consolidation of the underlying tissues. The percussion sound is duller and lower in pitch than on the left side. Upon aus-

cultation, the breath sounds are more remote and are diminished in intensity. Other pathologic changes, such as pleuritic exudation, râles and crepitation, are conspicuous by their absence. Furthermore, a history of lung trouble is not necessarily present. The location of the process at the lower posterior aspect of the right lung becomes better understood, according to the author, if the known fact is recalled that syphilis, in contrast to tuberculosis, usually involves the lower portion of the lung.

**Heart.**—By means of physical and fluoroscopic examinations, C M Kurtz and J A E Eyster (J A M A 95 440 (Aug 9) 1930) studied a group of syphilitic patients for cardiovascular involvement. Fifty-four patients had acquired and 12 congenital syphilis. Fluoroscopic evidence of syphilis was found in 90.7 per cent of the cases of acquired syphilis and in 30.4 per cent of those with congenital infection. Aneurism of the aorta was found in 18.5 per cent of all cases of acquired syphilis and was absent in all of the congenital cases.

No definite signs of syphilitic heart disease could be found by G. Previtali, Gertrude H B Nicolson, and D Moon-Adams (Am Heart J 6 128 (Oct) 1930) from a study of 28 girls and 22 boys with congenital syphilis, ranging in age from 4 weeks to 14 years, nor by T B Givan (*Ibid* 6.132 (Oct) 1930) from a similar study of 417 patients, ranging in age from 3 months to 42 years. Of the 939 patients with congenital syphilis studied by H McCulloch (*loc cit*), 458 were found to have recognizable heart disease. Of the total number of patients with congenital syphilis, 441 were in the first 2 years of life. It was possible to obtain necropsy examination on 32 children who died in

infancy. Three of these patients were found to have had syphilitic heart disease. None of the other 29 who died or the 409 who lived had symptoms at any time referable to the heart. Four hundred and ninety-eight of the syphilitic infants were over 2 years of age and of this number 5, or 1.0 per cent, were known to have heart disease. Two died but necropsy examination was not obtained. The other 3 children are still living. The signs of heart disease in the 5 children were similar to those in children with rheumatic heart disease but without syphilitic infection. The frequency of 1.0 per cent coincides with the frequency of 458 children (1.1 per cent) with heart disease among the total of 40,470 children admitted to the general clinic, or in other statistical surveys of the incidence of heart disease among normal or control children.

McCulloch concludes there is no evidence in the study that congenital syphilis contributes to the incidence of heart disease in children up to the age of 15 years. That heart disease and sudden death may follow this type of infection later in life is not made clear by the study, but it may be supposed that instances of this sequela would be almost equal to those that follow other acute infections.

**Stomach.**—J R Verbrycke, Jr (Am J Syph 13 524 (Oct) 1929) reports a case of a 13-year-old boy with congenital syphilis, who complained of epigastric pain and of vomiting. The physical examination was negative. Fluoroscopic examination revealed a shadow, with narrowing in the distal third of the stomach, producing almost an hour-glass picture. It was typically the sort of appearance expected in advanced malignancy. The condition, considered to be due to syphilis, im-



proved rapidly under antiluetic treatment

**Spleen.**—P. Lereboullet and R. Worms (Paris méd 2 400 (Nov 1) 1930) have observed that errors in diagnosis often occur when transitory *splénomégalies* in nurslings are accepted as symptoms of hereditary syphilis, whereas the hypertrophy of the spleen must be chronic and persistent to be of diagnostic aid. The authors have found that transitory splenomegalies often occur under the influence of a vaccinal eruption or a cutaneous suppuration.

**Kidneys.**—Anna Eljasz (Arch Dermat and Syph 22 274 (Aug) 1930) observed what appears to be a case of syphilitic glomerulonephritis in an 18-year-old girl with manifestations of late congenital syphilis, such as unusually generalized bone and joint lesions. The nephritis improved under an exclusive neoarsphenamine treatment.

**Suprarenals.**—Necropsy examinations of the adrenal glands were made by G. L. Fite (Bull Johns Hopkins Hosp 48 1 (Jan) 1931) in 250 cases of congenital syphilis. In only about 40 of the cases was any abnormality observed in the cellular structure of this gland, in some of these, striking syphilitic changes were present.

In virtually every case at his disposal in which spirochetes had been found, they were demonstrated in the adrenal gland. The presence of the spirochetes, however, was no indication of the probability of any pathologic alteration of the gland. Indeed, the most common finding of the adrenal gland was the presence of spirochetes without other changes. The simplest form of direct injury to the gland was necrosis. The most common finding was the occurrence of islands of blood-forming cells in the gland. In nonsyphilitic infants the

islands of blood-forming cells were rather small. What appears to be the most characteristic lesion of the suprarenal in congenital syphilis was that to which Simonowitsch has given the name "perihypernephritis syphilitica." This lesion was observed in 22 cases. In the more marked instances it consisted of an extraordinary amount of connective tissue in the capsule, which is very cellular and which contains no collagen fibers. Other inflammatory changes were also observed.

**Bones.**—*Osteochondritis, osteomyelitis, periostitis, and disturbance of growth* are changes which may occur in congenital syphilis.

**Osteochondritis.**—Osteochondritis occurred in 20 per cent of the early cases and in a somewhat smaller percentage of the late cases of congenital syphilis studied by E. D. Osborne and E. D. Putman (*loc cit*).

According to S. McLean (Am J Dis Child 41 363 (Feb) 1931), there seems to be an almost unanimous opinion among those who have written on osseous syphilis that in fetuses, as well as infants in the first few weeks of life, a deepening in the longitudinal axis of the provisional zone of calcification of the long bones, appearing on the x-ray as a white cap on the diaphyses and on the positive print as a dark metaphyseal band, is evidence of syphilitic involvement of the bones. It is the author's opinion that roentgenologists should be cautious about making a diagnosis of syphilis on this evidence alone.

In the author's experience, the next stage, in order of severity, of lesions at the epiphyses shows on the x-rays as a very slight or very marked degree of submetaphyseal rarefaction, either with or without the deepened provisional zone of calcification. In the first

months of life, when scurvy does not have to be excluded, the author knows of no disease other than congenital syphilis which will frequently produce this picture, although other conditions may very occasionally do so. The more advanced stage, characterized by the so-called zig-zag or saw-tooth metaphyses, according to the author, is the first evidence of lawlessness of growth, so characteristic of the active stage of syphilis.

According to A. H. Parmelee (Am. J. Dis. Child 39:673 (Mar) 1930), while there is similarity of the x-ray observation of the end of the long bones in scurvy and in syphilitic osteochondritis, there are differential points, which, when sufficiently evident, will prevent confusion. For example, in syphilitic osteochondritis, the distal margin of the epiphyseal line is irregularly serrated, the spongiosa is moth-eaten in appearance, often in striking contrast to the smooth, ground-glass appearance in scurvy. E. P. Pendergrass and R. S. Bromer (Am. J. Roentgenol. 22 1 (July) 1929) point out that the cartilage in scurvy is normal, while in both rickets and syphilis it is swollen. The epiphyseal center in rickets has a moth-eaten appearance throughout, with a partial or complete loss of the zone of temporary calcification, *ie*, the periphery. In syphilis the ring is intact, but localized areas of rarefaction within the center are often present, in close position or immediately adjacent to the periphery. In syphilis, furthermore, neither cupping of the diaphyseal ends nor lateral spurs can be found.

**Osteomyelitic Lesions**—Osteomyelitic lesions of several varieties, according to McLean (*loc cit.*), can be definitely diagnosed syphilitic by x-ray examination, especially if they are symmetrical. They are most frequently characterized

by rarefied, punched-out areas with thickened contiguous supportive periostitis, or punched-out areas shown by x-rays with destruction of the contiguous cortex. E. C. Vogt (Am. J. Roentgenol 26 96 (July) 1931) states that a special type of osteomyelitis, particularly as regards its location, is often seen as bilateral semilunar defects at the upper ends of the tibiae medially, adjacent to or just below the epiphyseal lines. This lesion occurred in 45 per cent. of his patients and was considered pathognomonic of syphilis.

**Periostitis**—McLean states that periostitis is seldom found as a sole lesion, and consequently is of less diagnostic importance than osteochondritis, which frequently occurs without periostitis. It may be assumed that there are 3 types of periosteal lesions, *viz* (1) periosteal thickening, occurring in an intact shaft independently of the lesions at the metaphysis; the lesion is generally thickest in the middle of the shaft, is not severe in character and is not associated with any demonstrable lesion of the spongiosa, (2) a supportive or healing type, found usually over any break in the cortex; (3) ossifying periostitis, the least common of the 3, characterized by a tremendous thickening of the entire shaft of the bone, resulting from a series of enveloping coat-like layers of new-formed bone.

M. Péhu and A. Policard (Rev franç de pédiat 6·50 (Jan) 1930) believe that the changes in the skeleton other than the long bones are of little interest clinically. However, G. K. Higoumenakis (Deutsche Ztschr f Nervenhe 114:288, 1930) calls attention to the frequent occurrence of the enlargement of the sternal end of the clavicle, a sign which he considers pathognomonic of syphilis. X-rays re-

veal an exostosis of the sternal end of the clavicle

**Growth Disturbance**—Growth disturbance, according to Vogt (*loc cit*), may be revealed only by a dense, narrow line at the ends of the diaphyses, but this is not diagnostic of syphilis, since similar lines may be seen as a result of arrest from any severe nutritional disturbance. In syphilitic children the line is usually associated with a parallel and proximal zone of diminished density.

G J Landa and V P Panow (*Ann de dermat et syph* 1.403 (Apr) 1930) observed that in syphilis there is a very definite retardation of the ossification of the wrist in 60 per cent of the patients. Their results seemed to show the definite dystrophic influence of the disease on ossification, even in infants, without clinical and serologic signs of syphilis, but born of syphilitic parents.

**Nervous System.**—From 20 to 30 per cent of children suffering from congenital syphilis show involvement of the nervous system, I A Abt (*J Arkansas M Soc* 25 213 (May) 1929). Mabel Masten (*J. Nerv and Ment Dis* 70: 379 (Oct) 1929) states that according to the source of material and the completeness of examination, statistics concerning the incidence of neurosyphilis range from 10 to 43 per cent. According to Abt (*loc. cit*), syphilitic endarteritis, meningitis, hydrocephalus, encephalitis, isolated gummas, local or diffuse sclerosis, cerebral and meningeal hemorrhage, juvenile tabes and paresis are lesions which may involve the nervous system in congenital syphilis. Epileptiform convulsions, deafness, polyuria, Fröhlich's type of adiposogenitalis, and according to F Ferguson and M Critchley (*Brit J. Child Dis*

26 193, July-Sept. 1929), mental defect and symptoms of the "parvulus child" may all be due to congenital syphilis. In a group of 50 patients studied by Ferguson and Critchley 32 per cent were diagnosed as general paralysis of the insane, 12 per cent as taboparesis, 14 per cent as tabes, and 26 per cent as belonging to the heterogenous group.

**Congenital Tabes**—F R Ferguson and M Critchley (*Brit J Child. Dis* 27 1 (Jan-Mar) 1930) maintain that congenital tabes is extremely rare. In this series of 8 cases of tabes the age of onset ranged between 10 and 24 years. The first symptoms were failing vision and the presence of paresthesia, while severe lightning pains, ataxia and sphincter disturbance were rare complications. Of the later symptoms, headache, photophobia and diplopia were the most common. Apart from slight mental dulness, no psychological abnormalities were observed. No cases of "crisis" occurred. Sensory loss and ataxia, in contrast with these manifestations in the adult, were slight.

The tendon reflexes were either absent or markedly diminished. Optic atrophy, strabismus and the typical pupillary abnormalities were common; nystagmus occurred in 3 patients.

**Dementia Paralytica**—Dementia paralytica, according to Masten (*loc. cit.*), is the most common form of congenital neurosyphilis. However, W C Menninger (*J A M. A.* 95:1499 (Nov 15) 1930) states that the incidence of juvenile dementia paralytica is probably under 1 per cent of all cases of dementia paralytica and under 2 per cent. of all cases of congenital syphilis. According to Menninger, some of the best evidence for a neurotropic strain of spirochetes can be marshalled from a study of the antecedents of young

patients with dementia paralytica. In 25 per cent of Menninger's cases the parents had symptomatic neurosyphilis. F. H. Leavitt (Arch Neurol and Psychiat 26:665, 1931) reported a case of juvenile dementia paralytica occurring in the third generation of a syphilitic family. The grandmother died of a tabetic type of dementia paralytica. The mother had congenital syphilis in infancy and childhood and in adult life had syphilitic disease of the optic nerve.

In Menninger's study of juvenile dementia paralytica the ratio of *male* to *female* patients was 1 to 16. The time of onset ranged between 6 and 16 years; in one of the patients the first symptoms appeared in the third year of life. There are 2 distinct types of onset. There may be a vague and indefinite development of the disease in the mentally and often physically inferior child, or the onset may appear as a more or less acute break after several years of normal development of the child.

**Symptomatology**—According to F. R. Ferguson and M. Critchley (Brit J Dis Child 27:1 (Jan-Mar.) 1930), dementia paralytica in the child differs from that in the adult in the following manner: (1) Early age of onset, (2) association with infantilism and with signs of visceral syphilis, (3) frequency of optic atrophy, (4) early appearance of bladder symptoms; (5) dilated and often totally inactive pupils, (6) contractures in arms and legs; (7) a different psychologic picture, (8) shorter course.

**Congenital Taboparesis**—Ferguson and Critchley point out that there is a group of patients with congenital neurosyphilis which, because of marked psychological changes, tremors and speech defects, cannot be placed in the

*tabetic* group. On the other hand, because of the absence of tendon reflexes and because of definite evidence of involvement of the posterior column of the cord, the patients cannot be regarded as cases of dementia paralytica. These patients the authors have classified as *taboparesis*, pointing out that this is the first time this term has been employed.

**DIAGNOSIS.—Compression Nystagmus Test.**—Attention is called by N. Asherson (J Laryng and Otol 46:326 (May) 1931) to the diagnostic value of the compression nystagmus test (Hennebert's phenomenon or "fistula symptom without fistula"). The sign is characterized by nystagmus to the opposite side when compression or aspiration of the external canal is made with Siegle's speculum, or compression by mere pressure of the finger over the external auditory meatus.

**Demonstration of Spirochæta Palida**—B. H. U. Mohrmann (Urol and Cutan Rev 34:48 (Jan) 1930) was able to demonstrate the *Spirochæta palida* regularly in the conjunctival secretions of young infants with congenital syphilis. The procedure, according to this author, offers an additional aid in the diagnosis of the disease.

**Serologic Tests.**—F. Paradiso (Clin pediat 11:245 (Mar) 1928) has concluded that the *D'Amato* reaction is inferior to both the *Wassermann* and the *Memcke* reaction in the diagnosis of congenital syphilis. G. Manace (Am J Dis Child 40:63 (July) 1930) performed a series of 1831 *Kahn* tests on children. Apparent clinical and serologic agreement was present in 1927 (97.3 per cent) instances in nonsyphilitic patients and in 39 (1.9 per cent) instances in syphilitic patients, making a total agreement of 1966 (99.2 per cent).

in which no false reactions were obtained. The *presumptive* procedure carried out in conjunction with the regular test, and differing from the latter in that it contains a modified or more sensitive antigen, was found to be of value as a serologic check, but apparently did not possess the specificity of the regular test. The author states that when a family history of syphilis is obtained or there is an indefinite history of stigma, the investigation should be prolonged in the form of repeated serologic examinations.

The presence of a weakly positive *Wassermann* reaction in the newly-born infant apparently does not necessarily signify a syphilitic infection in the baby. According to E. J. Trow (Canad. M. A. J. 23:48 (July) 1930), a reaction of this type may be due to the transmission of the "reacting substance" and not the *Spirochæta pallida* to the infant. F. A. Hemsath (Am. J. Syph. 15:396 (July) 1931) collected blood on the seventh day following delivery from 73 babies of mothers whose blood was positive on the prenatal examinations. Fifty-seven of the 73 were found to have blood fixation equal to or less than that demonstrated in the mothers' blood tests. Additional tests were made on 30 of the positive cases at the age of 1 to 2 months, or older. In 15 cases the Wassermann became negative without treatment, after having been positive on previous examination. In 3 cases the infants' Wassermann tests continued positive when retested at the age of 2 to 8 months. The 7 other patients had received treatment. While some authors (see Sajous's Analytic Cyclopedic of Practical Medicine, 10th Edit., Supplement 10:845, 1930) contend that the infant with syphilis will usually develop a positive Wassermann reaction at some

period during the first year of life and that it occurs more consistently in congenital than in acquired syphilis, the opposite view seems to be taken by other writers, particularly by French investigators (M. H. Grenet, Rev. de med. Paris 46:951, 1929). I. Quevrat (Bull. Soc. franç. de dermat. et syph. 37:378 (Mar.) 1930) contends that the medical profession as a whole needs instruction in regard to the frequency of a negative Wassermann test in infants with occult congenital syphilis.

*Stigmata*.—F. Herb (M. J. and Rec. 132:74 (July 16) 1930) considers a new *triad* of stigmata, consisting of palpable cervical nodes, scaphoid scapula and the "pulmonary sign," of considerable aid in the diagnosis of congenital syphilis.

**PROGNOSIS.**—R. R. Sullivan (Minnesota Med. 13:302 (May) 1930) concludes that the prognosis in general syphilis is generally *good*, as evidenced by leading authorities throughout the country. Sullivan's results were highly satisfactory from a clinical standpoint, but much less so from a serologic one. In a series of 60 patients, a reversal of the Wassermann was obtained in only 20 per cent., but of 20 with negative reactions on admission, 19 remained negative under treatment, leaving a total of 50 per cent. of the children with persistently positive Wassermann tests. The author states that some of the children included in the group with persistently positive reactions had been under treatment but a short time and that more reversals may eventually be expected. According to E. A. Morgan (Canad. M. A. J. 23:811 (Dec.) 1930), the physician's ability to obtain a persistently negative Wassermann test in congenital syphilis depends primarily on the stage of the disease in which treat-

ment is begun. In the early stage, 80 per cent can be cured, in the latent period, 64 per cent, while in the late stage of the disease, 49 per cent can be cured, provided the treatment can be administered for a reasonable period of time

**TREATMENT.—*Prophylactic.***—Recognition and treatment of the disease in the child, D M Pillsbury (Internat Clin 2:236 (June) 1931) contends, will not eradicate congenital syphilis, attention must be directed to the source of the child's infection, the syphilitic mother. The most important point of attack, in the opinion of Pillsbury (*loc cit*) and Sullivan (*loc cit*), is early diagnosis and adequate treatment of the syphilitic mother. E D Osborne and E. D Putman (*loc cit*) recommend that every pregnant woman should have a routine blood Wassermann and Kahn test. Pillsbury states that treatment of the pregnant woman seems to be tending away from conservative methods, the author recommending vigorous use of arsenicals in conjunction with bismuth. Trow (*loc cit*) feels that every syphilitic woman should be treated with salvarsan and mercury, or with salvarsan and bismuth during each pregnancy, without regard to the amount of treatment received in former pregnancies or between pregnancies. The occurrence of a negative Wassermann reaction in a known syphilitic, unless persistently negative over a period of years, should not be regarded as a contraindication to treatment. The best results, according to Pillsbury, are obtained by treatment from the beginning of pregnancy. Hoffman, according to Pillsbury, states flatly that adequate early treatment will assure a nonsyphilitic child. Many reports indicate, however, that treatment is still

effective if begun before the fifth month of pregnancy. During the last month, according to this author, treatment probably serves little purpose other than protecting the obstetrician from operative infection. However, many of Trow's patients were not treated until late in pregnancy, yet when the treatment was of a suitable type, the results were uniformly good.

***Treatment of the Infant and Child.***  
—*Acetarzone*—P von Kiss (Jahrb f Kinderh 126:211 (Jan) 1930) treated 18 patients with acetarzone. The drug was given by mouth in the following doses: daily dose of acetarzone during the first week of life was 0.06 Gm (1 grain); in the second week, 0.06 Gm (1 grain); in the third, 0.18 Gm (3 grains); and through the third month, 0.18 Gm (3 grains). The total amount given ranged between 15 and 20 Gm ( $\frac{1}{2}$  to  $\frac{2}{3}$  ounce). The symptoms of syphilis rapidly disappeared and the blood Wassermann reaction became negative in 7 of the cases. The only ill effects were vomiting and diarrhea. After an interval of 2 months, the administration of neoarsphenamine and bismuth was begun regardless of any changes in the Wassermann reaction.

***Bismuth***—L. B Dickey and T L Sutton (California West Med 31:242 (Oct) 1929) employ bismuth in the form of bismuth phenylformitate in doses of 15 mg ( $\frac{1}{4}$  grain) per kilogram ( $2\frac{1}{2}$  pounds) of body weight. Osborne and Putman (*loc cit.*) have replaced mercury with bismuth in their treatment routine. They recommend that the physician should know the content of bismuth metal in each ampule or cubic centimeter of the preparation used. The dosages of bismuth metal employed are as follows: first 4 weeks of life 0.02 Gm ( $\frac{1}{3}$  grain); 1 to 3 months old,



0.03 Gm ( $\frac{1}{2}$  grain), 3 to 12 months old 0.05 Gm ( $\frac{5}{8}$  grain), after 1 year of age, according to weight up to 0.1 Gm ( $1\frac{1}{2}$  grain)

J. F. Coppolino (Am J Dis. Child 39:288 (Feb) 1930) used bismuth exclusively in the treatment of congenital syphilis. He used a preparation of bismuth salicylate in oil suspended together with camphor and creosote, 1 c c (16 minims) of which contained 130 mg (2 grains) of metallic bismuth. The dosage employed was 65 mg (1 grain) for children under 1 year of age to 130 mg (2 grains) in older children. The course of treatment consisted of 20 weekly injections. A blood test was taken at the beginning and termination of each course, and if it was positive, the treatment was immediately continued; if negative, a 4-week rest period was allowed. The maximum number of courses administered was 3, after which the patient returned every month for examination and blood tests. The author concluded that bismuth in rather large doses is apparently well tolerated by infants and children.

Coppolino states that while bismuth is useful in the treatment of older children, it does not effect a cure. In young infants, on the other hand, bismuth therapy is most efficacious, rendering them both symptom-free and serologically negative.

Sullivan, in the treatment of 12 patients with positive Wassermann reactions, used bismuth extensively along with neosalvarsan over a period of years with the hope of producing a reversal of the reaction but without results.

While no absolute valuation of the drug can be made until several years have elapsed to determine the permanency of results, J. H. Stokes (Internat

Chir 2:241 [June, 1931], in a discussion of the treatment of syphilis in general, warns against the practice of substituting bismuth for the arsphenamines in the treatment of early syphilis, pointing out that the French are already paying the price for a practice of this type. Stokes contends it is the arsphenamine and not the heavy metals that control the infectiousness of syphilis.

*Malaria*—H. Koch (Wien klin Wchnschr 42:400 (Mar 28) 1929) used malaria therapy in 4 children with congenital syphilis. The patients did not show clinical signs of the disease, although both the blood and spinal fluid Wassermann tests were positive. The treatment, which was well tolerated by all the patients, ceased after from 7 to 9 attacks. Recovery was rapid and the reactions of the blood and spinal fluid Wassermann became negative. The author asserts that the treatment is especially suitable for those cases in which arsphenamine, mercury and bismuth do not bring the desired results. Masten (*loc. cit.*), as a result of the malaria treatment, observed definite mental improvement in one child with juvenile dementia paralytica. Osborne and Putman (*loc. cit.*) obtained excellent results with malaria therapy in 3 out of 5 children treated for juvenile paresis. It is their impression that in order to obtain good results treatment must be started early, before too much parenchymatous destruction has taken place. Koch states that in order to determine whether malaria therapy can actually prevent paralysis, a longer period of observation will be necessary.

**SYPHILITIC CARDIOVASCULAR DISEASE.** See CARDIOVASCULAR SYSTEM.

## T

**TETANY.** See CONVULSIONS

**TENTORIUM, SECTION OF.**

—Temple Fay (Surg Clin North America 10 1427 (Dec ) 1930) reports 5 cases in which the tentorium was sectioned from the incisura to the lateral sinus and included the lateral sinus for decompressive effects, in the presence of large *posterior fossa tumors*

Formerly, suboccipital decompressions gave expansion of the tumor posteriorly but offered no relief from the strangulation of the aqueduct and the brain stem at the level of the incisura. The bone flap was divided so as to expose the lateral sinus and occipital poles of the cerebrum as well as the cerebellar fossa. The dura was opened over the cerebellar area after ligation of the occipital sinus and the dural flap was opened over the occipital pole above the lateral sinus. The occipital lobe was elevated, the emissary veins ligated and the tentorial roof exposed. Advancing along the roof of the tentorium to the incisura, the tentorium was sectioned from within out, exposing the cerebellum below the cerebellopontile angle and permitting ample room for removal of the deep lesions in this area, as well as a most satisfactory form of decompression, the results of which have proved to be far more satisfactory than the former suboccipital decompression alone. The lateral sinus has been ligated where this proved to be small and unimportant, giving rise to complete freedom from dural constriction where medulloblastomas and gliomas have been encountered.

**THORACOPLASTY.** See TUBERCULOSIS, PULMONARY. SURGICAL TREATMENT.

**THROMBOPHLEBITIC EDEMA.—ETIOLOGY.**

—A series of experiments on the hind legs of dogs was performed by L M Zimmerman and G de Takats (Arch Surg 23 937 (Dec ) 1931) in an effort to determine just what was necessary to produce thrombophlebitic edema. It was determined that removal of all of the iliac lymph glands, together with the retroperitoneal fatty and areolar tissues from the bifurcation of the aorta to Poupart's ligament, did not produce edema; nor did it result from ligation of the common and internal iliac veins in the limb which had been thus treated.

Edema may be produced by the injection into the femoral vein of a bland substance capable of causing the blood to clot, such a substance is either the serum from the clotted blood of the animal being experimented upon, or the tissue extract sold under the trade name of fibrogen. Edema thus caused is not dependent upon obliteration of the lymphatics, because when limbs showing this edema were given injections of india ink into the foot pads, 24 hours later ink discoloration was observed in the inguinal lymph glands.

It is proven that the quality of the injected substances does not cause the resultant edema, because these substances were injected into the ligated vein with heparin, which prevented extensive clotting, and no edema ensued therefrom, whereas the substance injected alone produced extensive clotting, which was followed by marked edema of the limb.

The extent of the thrombosis is thus shown to be the factor upon which edema depends in any given case of venous obstruction, as ligation alone (as has been shown by Homans and others)

of the main veins of the limb does not result in edema

**THYMUS GLAND.—HYPER-TROPHY.—*Diagnosis.***—Of timely interest is the article of R L J Kennedy and G B New (J A M A 96 1286 (Apr 18) 1931), which describes the mistaken diagnosis of enlarged thymus when further examination reveals that the symptoms are the result of another condition. The authors find that stridor, hoarseness, dyspnea, cyanosis, wheezing and noisy respiration are usually the result of other than thymus enlargement. The numerous deaths in juvenile surgery are often unjustly attributed to thymus hypertrophy. Attention should be given to the preoperative care of those children who show evidence of infection of the upper respiratory tract, fever, anemia, cardiac and renal disease, malnutrition, gastrointestinal disease and other conditions which might increase the operative risk.

H K Pancoast (Am J M Sc 180 745 (Dec ) 1930) states that the thymic menace in infants and young children is largely a matter of tracheal stenosis with relaxation of the soft tissue of the upper respiratory tract. The most serious complication is paralysis of the recurrent laryngeal nerve. The only definite signs of an enlargement of the gland are an abnormal narrowing and buckling of the trachea at the thoracic inlet as it passes over the apex of the chest and the lateral deviation of the trachea which is shown in the sagittal view. The roentgenologist must remember to distinguish foreign bodies, the effects of obstructive specific laryngeal infections on the lumen of the larynx, postdiphtheritic and other forms of acquired or congenital stenosis, retropharyngeal and retrotracheal abscesses,

adenoids, atelectasis and unusual collapse of the soft tissues.

***Treatment.***—The treatment of the enlarged thymus in infants and young children is markedly influenced by the **x-ray**, according to Pancoast (*loc cit*), because this special tissue is extremely sensitive to irradiation. The dose, therefore, should be the minimum to produce therapeutic effects. Factors influencing the dosage are the age and size of the child and the thickness of the chest wall. With extremely small doses only the thymic area is irradiated, preceded by a thorough physical examination of the chest and neck.

When symptoms persist and after the first small dose, a second application is given after a week. The average number of applications in cases without recurrences is 2, but these recurrences occur in a fairly large percentage of cases.

**CANCER.**—M Baer (Schweiz med Wchnschr 60·732 (Aug 2) 1930) has reviewed 54 proven cases of cancer of the thymus gland reported in the literature to the present time. The tumor is found to occur most commonly in the male in middle or advanced years. It usually develops in the anterior mediastinum and simulates infantile thymus. In one-third of the cases it metastasizes outside of the thoracic cage.

**THYROID GLAND, DISEASES OF.—GOITER.—*Etiology.***—Four epidemics of goiter have been described in Russia up to the present time and V Oppel (Vrach gaz 34·199 (Feb 15) 1930) reports an epidemic in a portion of the military forces of Leningrad which was of interest because neither endemic nor epidemic goiter had previously been described there. In most instances, the goiter was

associated with sweating, increased irritability of the heart, a low arterial pressure and a lymphocytosis of the blood. Tracheitis was demonstrable in many cases. Hypoglycemia was present in 11 of 20 cases, and the alkali reserve was low.

Excised fragments of tissue showed a parenchymatous goiter with proliferating epithelium and colloid liquefaction. The iodine content of 4 of 5 goiters was about 20 mgm ( $\frac{1}{3}$  grain) per 100 grams ( $3\frac{1}{3}$  ounces).

From these observations, the author concludes that the basis of the disease is a hyperfunction or dysfunction of the thyroid, associated with a hypofunction of the insular apparatus and a dysfunction of the hepatic system.

Infection from the upper respiratory tract was the probable etiological factor, as the removal of the patient from a locality, with improvement of the infection, usually resulted in a marked improvement in the condition of the thyroid.

Regarding *endemic* goiter, J. Wagner-Jauregg (Wein. Klin. Wchnschr. 43:1 (Jan. 2) 1930) differentiates 2 types of goiter, the one which occurs in the mountainous districts of the Alps, and the other at lower altitudes along the ocean. The former goiter is of the parenchymatous type, while the latter is a colloid form. Goiter of the newborn is not observed in low altitudes but is common in the Alps. Those patients having colloid goiter are susceptible to iodine.

**Prophylaxis.**—In a study of the prophylaxis of goiter, W. Weston (South M. J. 23:479 (June) 1930) believes that the solution of the problems of goiter will be in an adequate diet which is rich in iodine, iron, manganese, copper and perhaps other mineral

salts. He states that since goiter does not exist in either animals or human beings when fruits, vegetables and milk are rich in these products, he concludes that if during such conditions as gestation, lactation and menstruation, a relatively larger amount than usual is consumed, goiter will no longer be a problem.

In a review of the literature on the prophylaxis of goiter, F. de Quervain (Schweiz. med. Wchnschr. 59:1099 (Nov. 2) 1929) finds that harmful effects from the use of iodized salts are only reported by American authors. He explains this on the basis that the salt used in America contains from 40 to 100 times as much iodine as that used in Switzerland. To many individuals who are hypersensitive to iodine, the American form is injurious. For the same reason he believes the small amount of iodine in the Swiss salt is not enough to be harmful to the most susceptible case.

**Treatment.**—The observations of G. E. Pfahler and J. H. Vastine (Am. J. Roentgenol. 24:395 (Oct.) 1930) in a large series permit the conclusion that **x-ray** therapy offers as great prospects of cure or marked improvement as can be obtained from any other known means. In cases in which there is pressure or embarrassment of respiration, **surgery** is definitely indicated. When medical treatment fails or surgery is refused, the nontoxic cases may be given small treatments with little danger of impairment of the normal function of the gland.

**Results of Surgical Treatment.**—G. M. Curtis (S. Clin. North America 10:313 (Apr.) 1930) finds that the trachea following removal of the *intrathoracic* goiter returns to its normal position in about 8 weeks. This type of goiter is

usually nodular and occurs more frequently on the left than the right side, probably because of the position of the innominate artery and the superior vena cava. They tend to grow and undergo cystic degeneration, especially vascular changes with hemorrhages. Ultimately they may undergo malignant changes.

**GRAVES'S DISEASE.—Etiology.**—Graves's disease is regarded by E. Moschcowitz (Arch Int Med 46:610 (Oct) 1930) as a syndrome of disorders with a history extending over a long period of time, which is characterized by a sensitive, emotional, neuro-pathic personality often showing familial and hereditary tendencies, and is strongly influenced by environment. Moschcowitz considers that there is no basis for the opinion of the close relation between the thyroid and thymus glands. Undoubtedly, the basic factor is *fear* and the changes in the gland are a result, and not the cause, of the disease, but are probably the result of the influence of the nervous system. The author has found that the disease is most prevalent in those races of a highly emotional type.

D. Marine (Am J M Sc 180:767 (Dec) 1930) supports the theory that a deficiency of some internal secretion of the suprarenal gland and sex glands is one of the fundamental factors in the etiology of Graves's disease and that the thyroid changes are actually representing a compensatory mechanism, although often an injurious one.

Those cases which occur early in life he would concede belong to the constitutional defect of status lymphaticus; while those cases developing around the decline of sexual life belong to a group in which the constitutional defect may be acquired.

In the cat and rat, according to

Marine, it is possible with a sublethal injury to the suprarenal glands to bring about a temporary syndrome which closely resembles Graves's disease. A somewhat similar condition to that developed in suprarenal injuries occurs normally in newborn infants where there is an involution of the suprarenal cortex. This cortex is unduly large and begins to involute about the eighth day of extrauterine life. For the next 4 weeks there is a marked reduction in the size of the cortex. There is during this time a decided increase in the rate of heat production.

In the treatment of these conditions, Marine has found that the administration of a **glycerol emulsion** of the very **fresh ox suprarenal cortex** causes a striking gain in body weight and in muscle strength. This change after 2 weeks of feeding could not be obtained with the dry preparations. From these studies, Marine and his workers believe the cortex produces a substance which tends to regulate or control thyroid activity which is deficient in Graves's disease, whereas the medulla produces a very powerful activator of the thyroid secretion which is not impaired in the developmental stages of the disease.

In a summary of his work upon the etiology of goiter, including Graves's disease, David Marine (Ann. Int Med 4:423 (Nov) 1930) states that thyroid enlargement in goiter is apparently always due to a *deficiency of iodine in the gland*. On the other hand, this deficiency may be primary or secondary. Thus the amount of iodine may be normal, but increased demands make it impossible to produce the necessary amount and hypertrophy results.

Iodine is also classified as a direct antigoutrogenic substance in that it is essentially a constituent of the thyroid

hormone and, therefore, prevents goiter by making it easier for the thyroid to produce an abundance of thyroxine

These goiters, the result of a primary or absolute deficiency of the iodine, are definite and easily understood, whereas those due to a secondary iodine deficiency are not so easily understood. So much emphasis has been placed on iodine deficiency in the etiology of goiter that there is a tendency to forget to bear in mind that the iodine deficiency may be either primary or secondary

**Pathology.**—A most interesting series of observations on the *carbohydrate metabolism* of thyroid cases has been compiled by B Kugelmann (Klin Wchnschr 9:1533 (Aug 16) 1930), in which he performed the glucose tolerance test on normal individuals and patients with exophthalmic goiter. He found that the height of the blood sugar was much above normal in the latter group and also that the return to normal was much slower in these individuals. On the basis of these observations the author concludes that in the liver in thyrotoxicosis, the glycogen deposits are depleted and the liver is no longer capable of changing large quantities of levulose into dextrose and storing it. This plainly demonstrates that in exophthalmic goiter there exists a functional disturbance of the liver which becomes manifest in the pathologic behavior of the intermediate carbohydrate metabolism

Frequent occurrence of diffuse fatty degenerative infiltration of the liver in patients dying of exophthalmic goiter has been noted by C V Weller (Editorial: Ann Int. Med 4:501 (Nov) 1930). The process resembles that seen in severe toxic processes, such as phosphorus poisoning. Autopsies were done on 44 patients dying of Graves's dis-

ease. Cases of cholecystitis, syphilis and other related conditions were excluded. Well marked chronic hepatitis was found in 22, slight or moderate hepatitis in 16, and no evidence of hepatic change in 6. Forty-four controls of the same ages, with the same complications being excluded, but not having Graves's disease showed marked hepatitis in only 1 case, slight or moderate involvement in 13, and no hepatitis in 30. The author concludes that the coincidence of hepatitis with exophthalmic goiter is, therefore, significant and is in accord with clinical observations of the occurrence of functional disturbances of the liver in Graves's disease

Weller quotes several clinical investigations of liver function in this disease, as well as some results of animal experimentation. J B Youmans and L M Warfield (Arch Int Med 37:1 (Jan) 1926) demonstrated liver dysfunction in 50 per cent of 44 patients with thyrotoxicosis by clinical tests. J P Simonds and W. W Brandes (Arch Path 9:445 (Feb) 1930) found that the livers of dogs with thyrotoxicosis were practically devoid of glycogen, and Abeling, Goldener and Kabori demonstrated that animals fed thyroxine no longer formed glycogen unless a high fat diet was given. The author suggests that this disturbance of glycogen metabolism may be responsible for the liver damage found in exophthalmic goiter

A J. Abbott and F W Van Buskirk (Am J M Sc 182:610 (Nov) 1931) were able to produce a fatal hypoglycemia in a rabbit with epinephrin, following thyroid gland feeding for 3 weeks. This confirmed the observations of Burn and Marks that thyroid extract feeding depleted liver glycogen in rabbits. Abbott and Van Buskirk were unable to produce similar results in cats



and dogs, probably due to the great resistance of these animals to thyroid feeding

A study of the size of the *heart* in goitrous individuals has always been an interesting problem and L. M. Huxthal, O. J. Menard and M. E. Bogan (Am J M Sc 180 772 (Dec) 1930) have made teleoroentgenograms from a series of 100 consecutive cases of nontoxic goiter. No definite relationship could be found between the duration of the disease or the loss of weight and the size of the heart. Cardiac enlargement was fairly coincident with age and cardiovascular disease. The number of enlarged hearts of different degrees was practically the same for the toxic and nontoxic groups. Thus, it is suggested by the authors that if hyperthyroidism causes cardiac enlargement or hypertrophy or dilatation it is slight.

**Symptoms**—J. Parkinson and H. Cookson (Quart J Med 24 499 (July) 1931) also made a study of a series of *hearts* of goitrous individuals and they found that the form of the heart is often affected in a characteristic way in this disease. From postmortem examination, they found that when the symptoms and signs of thyroid disease are of short duration, there were very few changes in the size and shape of the heart. The greatest enlargement was seen in those cases with auricular fibrillation and failure. The author believes that x-ray evidence of cardiac enlargement is an indication rather than a contraindication for surgical intervention.

J. C. Ruddock and C. G. Toland (Am J Surg 8 975 (May) 1930) stress particularly the importance of the cooperation between the cardiologist and the surgeon in the treatment of *thyroid hearts*. They believe this type of heart shows a functional disturbance

which cannot be cured unless the causative agent, thyroid disease, is eliminated. Such a heart will eventually become decompensated. Palpitation, tachycardia, dyspnea and general muscular weakness are not heart signs, but only evidence of the sympathetic neurosis accompanying the thyroid disease. As in a nonthyroid heart, *digitalis* is only of value in the presence of decompensation and the digitalization should be promptly and completely attained. According to the authors, the effect of *digitalis* to lower the cardiac output before the operation is often the deciding factor in the end-result of the surgery and the operation should not be delayed for any period after compensation has been established.

**Complications.**—The relationship between the glands of internal secretion and certain types of *dermatosis* is little understood. Myxedema resulting from hypofunctioning of the thyroid gland is the best known clinical picture. Hyperfunctional disturbances are less frequently recognized. P. A. O'Leary (Arch Dermat and Syph 21 57 (Jan) 1930) reports 8 cases in which non-pitting, edematous, tawny *plaques* developed in the lower extremities in association with hyperthyroidism. The features common to all are acute hyperthyroidism of moderately severe degree, longstanding edema of the extremities of cardiac origin, and tawny *plaques* that were not influenced by the therapeutic measures which brought about improvement in the symptoms of hyperthyroidism.

The microscopic picture is that of a marked degree of myxedema, although the clinical picture in each case at the time of the development of the *plaques* was one of acute hyperthyroidism. No explanation is offered at this time of the mechanism involved. The expression

"localized myxedema" is avoided because the term myxedema is now in common usage applicable to the group of constitutional symptoms which develop as a result of hypofunctioning of the thyroid gland and of which the cutaneous manifestations are merely a coincident of race. The study of this series of cases has precipitated a more extensive investigation into a combined physiochemical microscopic study of the changes in myxedema.

Measures directed toward the treatment of hyperthyroidism had no influence on the edematous plaques. Surgical excision of the plaques gave fairly satisfactory results in 1 case (a young woman). In 3 of the cases the lesions have undergone spontaneous involution, the remnant of the plaques is lichenified, slightly pigmented and raised after 3 years.

K. E. Bach (Deutsche Ztschr f Chir. 222:1 (Jan) 1930) analyzed 60 cases of exophthalmic goiter submitted to surgery. Seven fatal terminations had *cardiac symptoms* as dominant features. In 6 cases the presence of a *status lymphaticus* was noted. Of the 53 who survived, only 10 were found to have pathology in the heart. The author concludes that all deaths in his series were heart deaths. Many of the cases were in the early stages of decompensation. He believes the reaction against large doses of iodine is of value in the differentiation between thyrotoxicosis and exophthalmic goiter. The basal metabolism is a determination of doubtful differential value. The author stresses the importance of examination of the heart preoperatively if fatal endings are to be avoided.

From a study of the association of exophthalmic goiter with *pregnancy*, H. Kustner (Zentralbl. f Gynak. 55 578

(Mar 7) 1931) concludes that during pregnancy, especially toward the end of term, the functioning of the thyroid decreases. In women with hyperthyroidism it has the effect of partially counteracting the hyperfunction and the patients feel better, while in those women who have hypothyroidism, the symptoms are aggravated.

**Diagnosis.**—G. Bulmann (Hospitalstid 74 395 (Apr 2) 1931) found that the iodine content of normal individual's blood was 0.008 to 0.018 mgm per 100 c c. While those patients with nontoxic goiters showed no change, those with thyrotoxicosis had a content increased to 0.01 to 0.154 mgm per 100 c c. The author suggests that determinations of the iodine content of the blood may make it possible to diagnose exophthalmic goiter before there is any definite increase in the basal metabolism.

L. M. Hurxthal (Arch Int Med 47 167 (Feb) 1931) has made an exhaustive study of the preoperative and postoperative blood-pressure readings of thyroid patients. The author found that the blood-pressure of these patients under basal conditions is much lower than that of normal patients under similar conditions. The pulse pressure was found increased in thyroidism and decreased in about 50 per cent of the cases following relief from thyrotoxicosis. There was no definite relation between the height of the blood-pressure and the basal metabolic rate. The average basal blood-pressure readings following relief from the hyperthyroidism in exophthalmic goiter and from toxic adenomatous goiter was approximately the same in all age groups up to 50 years, but thereafter it was slightly higher in the toxic adenomatous groups. The blood-pressure in hypertension complicated by hyperthyroidism underwent on

the average the same changes that the patients with hyperthyroidism without hypertension underwent following operation. In hypertensive patients with auricular fibrillation and hyperthyroidism, the average blood-pressure is higher after operation when thyroid toxicity has been relieved and the normal restored. There was no evidence, from the study, from which it could be concluded that hyperthyroidism leads to permanent cardiovascular hypertensive disease.

S. A. Levine (Ann Int Med 4 67 (July) 1930) calls attention to the large number of patients who are treated for heart disease in whom the underlying cause is a latent and unrecognized hyperthyroidism. These cases are frequently overlooked, according to the author, because the typical signs of exophthalmos and toxic adenoma are not present. If a definite heart lesion does exist, it makes the diagnosis just that much more difficult. In many instances, almost complete relief from typical anginal attacks may be anticipated from the proper handling of the thyroid dysfunction.

"Borderline" cases of thyroid disease are always interesting and intriguing. J. K. McGregor (Canad M A J 25 152 (Aug) 1931) reports a case in which the patient complained of pain over the right chest posteriorly, dyspnea, general malaise, cough, nervousness, hoarseness and palpitation. He presented a generalized cardiac hypertrophy with arrhythmia, a blood-pressure of 200 over 140 and a basal metabolic rate ranging from plus 61 per cent to 85 per cent. Lugol's solution was of no avail and the patient died in a comatose condition.

The autopsy revealed no pathology, micro- or macroscopically, of the thyroid, but a suprarenal tumor about 6

cm in diameter which was undergoing yellow atrophy. The absence of a palpable thyroid, also the absence of tremor and loss of very little weight, with a high basal metabolic rate, made the case seem puzzling. The futility of Lugol's solution led away from the diagnosis of hyperthyroidism.

**Treatment.**—W. O. Thompson, P. K. Thompson, A. G. Braley and A. C. Cohen (Arch Int Med 45 481 (Apr) 1930) believe the moderately severe and mild cases of exophthalmic goiter may be treated with iodine alone. In mild cases the incidence of unsatisfactory results is so small that it is not a contraindication to continuation of the treatment. The author points out the possibility of a normal regression during the administration of the iodine.

A series of 100 women with hyperthyroidism was studied by W. Raab (Wien klin Wchnschr. 44 309 (Mar. 6) 1931). This number equalled 52 per cent of all the women examined in the university, giving an idea of the prevalence of thyroid disease in Vienna. In 37 of the cases it was found that the administration of iodine had either caused or exacerbated the hyperthyroidism. The importance of iodized salt is brought to prominence when it was found that 44 of the cases were using it. Thus it may be truthfully stated that neither its harmlessness nor harmfulness has been established beyond a doubt.

It is the opinion of J. Remer and W. W. Belden (Radiology 14 145 (Feb.) 1930), that certain patients with toxic goiter should be given the benefit of irradiation for at least 4 treatments. If no benefit is self evident, then surgery must be considered. The authors do not believe that irradiation increases the difficulty of subsequent surgery, but rather consider it to be beneficial. There

is little danger of hypothyroidism, the basal metabolic rate being a valuable adjunct and guide to the use of the x-rays

In commenting on the result of radium treatment, F Hogler (Wien klin Wchnschr 44 180 (Feb 6) 1931) reports that of 306 patients with exophthalmic goiter or with hyperthyroidism who in the course of 12 years received radium treatment, 217 showed marked improvement, 46 showed slight improvement, and 43 cases had no benefit. No exacerbations of the condition were found as a result of the use of radium. Many observations by numerous careful investigators have failed to reveal anything but a few fine adhesions which are of no consequence or importance.

A Lorey (Deutsche med Wchnschr 56:259 (Feb 14) 1930) believes the use of the x-rays in thyroid cases is less spectacular and slower but is less dangerous than surgery. He explains that complete observation in each case must be made, rather than placing complete confidence in the basal metabolic rate as a measure of the severity of the case. He warns against the continuation of the irradiation after the rate has reached normal, for fear of the development of hypothyroidism and myxedema.

Many workers have been attempting to obtain beneficial results from the use of animal blood injections in cases of Graves's disease. A Zimmer (*Ibid* 56 608 (Apr 11) 1930) treated 120 persons in this manner. The injections were made with fresh defibrinated blood of sheep and bovines, the 2 types being used alternately. At each treatment 3 to 5 cc was injected into the gluteal muscle. The usual requirements were from 3 to 5 treatments. Sweats, tremor, loss of hair and diarrhea were the symp-

toms and signs most benefited. The weight increased and the metabolic rate decreased. The author points out that the animal blood therapy is contraindicated in those cases in which there is great loss of weight, and in these instances he advises high caloric diets with insulin first.

**Surgical Treatment.**—N E Clarke and I Black (Arch Int Med 46 266 (Aug) 1930) make a definite and concerted plea for a more careful preoperative selection of patients for thyroidectomy. They studied a series of 181 patients and found 70 per cent lost weight following the operation, which surely was not gratifying. Hence they considered surgical intervention in the majority of their cases quite unsatisfactory. They believe that surgical intervention is only a substitution therapy, substituting the dominant myxedema for the less dominant state of hyperthyroidism, and not in any way altering the real constitutional condition, but only alleviating it. According to these writers, a perfect surgical result depends on the chance development of a perfect equilibrium between the hyperthyroidism and the myxedema.

In considering the risks of surgery to the thyroid patient, J. K. McGregor (Canad M A J 24 397 (Mar) 1931) lists the following:

Major factors which influence the thyroid risk

1 Visceral changes—an uncertain quantity.

2 Crises—controlled by Lugol's solution

3 Nerve injury—controlled best under local anesthesia

4 Time, place and type of operation—determined by type and cooperation of the patient plus the judgment of the surgeon.

Minor factors which influence the thyroid risk

1 Preoperative preparation (a) Rest, (b) forced feeding, (c) liquids

2 Operation (a) Careful control of hemorrhage, (b) protection of laryngeal nerve, (c) washing wound with antiseptic solution

3 Postoperative treatment (a) Rest, (b) medication, (c) use of steam, (d) use of rectal irrigations

*Injuries to Laryngeal Nerve*—M Nordland (Surg Gynec Obst 51 449 (Oct) 1930) states that since Kocher called attention to the fact that the interarytenoid muscle is supplied by the internal branch of the superior laryngeal nerve and since the author's dissections indicate that it is easy to injure the superior laryngeal nerve in the ligation of the superior thyroid artery, it is reasonable to conclude that postoperative disturbances of the voice may occur from an injury of this nerve. Further, because the recurrent laryngeal nerves occur anterior to the inferior thyroid arteries just as frequently on both sides, and because they penetrate the thyroid space a little farther from the tracheoesophageal groove than is usually described, therefore, to avoid injury to these nerves, extrafascial ligation of the inferior thyroid artery, according to the work of de Quervain, is more reasonable when ligation of this artery is contemplated.

In a plea for more careful surgery upon the thyroid with the attendant injury to the laryngeal nerves, A H Noehren (New York State J Med 31 410 (Apr) 1931) states that the posterointernal portion of the thyroid lobe left behind should not be disturbed by folding the raw surface over on itself. This is not necessary and is apt to compress the nerve. Removal of the second

lobe should not be undertaken until there is reason to believe that the nerves on the opposite side have not been injured by removal of the first lobe.

According to C F Dixon (Ann Surg 90 982 (Dec) 1929), a permanent injury to one laryngeal nerve gives little or no postoperative trouble. A severe tracheitis plus a unilateral injury may result in respiratory embarrassment for 2 or 3 days. Edema of the glottis plus injury to the nerve causes a narrowing of the breathing space. The uninjured cord will move laterally on inspiration. The treatment of such a case of *respiratory obstruction* due to a nerve injury consists in the use of an **oxygen tent** and the application of **hot moist dressings**. **Tracheotomy** may be necessary because of obstruction and cyanosis, but the tube may be removed when the cords move normally.

*End Results of Surgical Treatment*—F H Lahey (Surg Gynec Obst 50 139 (Jan—No 1A) 1930) concludes that thyroidism in itself does not by its direct action on the heart produce destructive changes. Of the 101 thyrocardiac patients operated on and now living, 76 have full return of function enjoyed before the onset of hyperthyroidism, while 19 have persistent auricular fibrillation and 9 are completely disabled.

M G. Gillespie (Minnesota Med 13 235 (Apr) 1930) reports the findings on the follow-up of a series of 200 cases subjected to thyroidectomy for goiter over 1 year, but not more than 7 years previously. In 25 (8 per cent) a definite hypothyroidism or myxedema was present with the basal metabolic rate of minus 15 to minus 44 per cent.

Twenty patients with rates from minus 10 to minus 15 were not materially benefited by thyroid medication and

their chief complaints were weakness and fatigue. They had a low rate and edema. The author drew the following conclusions:

1. Persons operated upon for goiter should be subjected to a more careful study especially as regards the metabolism.

2. In all cases of definite hypothyroidism, proper thyroid medication will cause improvement.

C. S. D. Don (Brit. M. J. 2: 287 (Aug.) 1931) gives the details in 42 cases of toxic goiter in which operation was performed and gives the method of examination. From his observations he believes the disappearance of exophthalmos does not of necessity follow the complete relief of hyperthyroidism, yet a diminution of toxicity is usually attendant upon an improvement in this sign. This sign is frequently persistent, especially in those cases in which the basal metabolism does not completely return to normal. Nervousness is certainly benefited by the operation and many patients gain weight following it. Failure to gain weight is often the result of a glycosuria. Although a normal metabolic rate may be obtained by a simple operation of ligation of the thyroid arteries, this operation will have little effect upon the final outcome of the case.

**Postoperative Reaction.**—An extensive survey of cases of exophthalmic goiter was made by Artur Bier (Klin. Wchnschr. 9: 819 (May 3) 1930) in an attempt to explain the etiology of the postoperative reactions. The popular opinion was that the traumatism of the operation placed in the circulating blood larger amounts of thyroid secretion, but this is not the case. The author found that the content in the blood was 5 to 10 per cent less following the operation.

He concludes, therefore, that the postoperative reactions are the result of a lack of the proper amount of thyroïdal secretion after the operation. Thus, he makes a plea for the substitution of iodine in the treatment of these cases.

In spite of all other forms of therapy, surgeons feel that the only satisfactory treatment of these cases is surgical. In most instances they advise a one-stage operation, but in those cases in which there is marked loss of weight and strength, and the patient does not react well to preoperative medication, it is wiser to do a two-stage operation.

**Operative Mortality.**—Discussing the operative mortality in 2769 cases of hyperthyroidism treated surgically at the Lahey Clinic from 1925 to 1929, H. M. Clute (J. A. M. A. 95: 389 (Aug. 9) 1930) reports 2128 cases of primary hyperthyroidism in which there were 14 deaths and in the toxic adenomata, numbering 641, there were 12 deaths.

Of the 26 deaths, 19 were the result of postoperative intensification of the thyroid intoxication; 3 to emboli; 2 to mediastinitis, 1 to pneumonia, and 1 to typhoid.

Previous to 1925, all cases were treated by multiple stage operations. In 1925 these were superseded by preoperative preparation with iodine, followed by a one stage operation. As the mortality began to rise, a change was made to the multiple stage operation, whether iodine was used or not. By this means the mortality was reduced to a minimum.

**HYPOTHYROIDISM.—Symptoms.**—The symptoms of myxedema plainly suggest to the keen observer hypothyroidism, according to C. E. Starns (U. S. Vet. Bur. M. Bull. 7: 564 (June) 1931), but the symptoms in the milder forms of hypothyroidism are less characteristic and cause considerable dif-



ficulty in arriving at the proper conclusion. Most observers believe the lowered basal metabolism is the most common single evidence of hypothyroidism and for this reason, when a patient who has such a rate complains of a tired worn out feeling, loss of strength, loss of weight, nervousness, vague pains and similar symptoms that cannot readily be accounted for, the possibility of hypothyroidism should be considered seriously.

**CANCER.**—P. F. Shapiro (Ann. Surg. 92 1031 (Dec.) 1930) reports a case observed at necropsy in which thyroid nodules were scattered over the omentum and the peritoneal surface of the intestine and also in the ovaries. The patient had an adenoma of the thyroid but these nodules had apparently not developed from a metastasizing adenoma. He believed the origin was an abnormally placed embryonal thyroid anlage.

In an article by I. Levin (Am. J. Path. 6 563 (Sept.) 1930) a plea is made for a careful search for the primary growth in all cases of bone metastasis of carcinoma. He believes that in the female, next to the breast, the thyroid should be suspected, and in the male, next to the prostate, the thyroid should be considered as a possible source.

R. A. Willis (*Ibid.* 7:187 (May) 1931) reviews the literature of 47 cases of metastatic neoplasms of the thyroid and then adds 10 of his own. He believes that different types of tumors have different tendencies in establishing metastases in the thyroid and he warns particularly concerning the melanoma and the lung carcinoma as the most potent in this respect. He has also found that edematous areas of the thyroid are much more prone to harbor

metastatic growths than normal thyroid tissue.

**THYROID AND HEART DISEASE.** See **CARDIOVASCULAR SYSTEM**

**TONSILS.—BACTERIOLOGY.**—Strains of streptococci in tonsils of healthy persons were found by Utevskaya and Pekker (Russ. Kaya Oto-Laryngol. 23 422, 1930) who state that among the bacteria of the oral cavity, streptococci are those which at present attract the utmost attention of all modern investigators on this subject. It is easy to understand if the number of illnesses provoked or complicated by them are taken into consideration, as well as the volume of research work on cryptogenic infection, in which streptococci play the main part. The importance of streptococci in the pathogenesis of tonsillar infections was confirmed lately by the work of many American authors. Nichols and Bryan found streptococci in 75 per cent of all tonsils removed, Pilot and Davis in 97 per cent, Bell in 70 per cent, etc. All the observers studied not only the frequency of streptococci in the tonsils but also their various characteristics, yet the description of the species of different streptococci was entirely omitted. The authors not only endeavored to give a bacteriologic description of each group of streptococci revealed, utilizing the technics of Klimer, Worth and Pesch, but also studied them from the morphologic and cultural, as well as the biochemical and pathogenic aspects.

The biochemical characteristics of the streptococci were investigated by their ability to split carbohydrates and fats. The experiment included 104 cases of absolutely healthy persons without any evidence of tonsillitis or any other visible lesions in the oral cavity. Bac-

terioscopically the streptococci were discovered in 48 per cent of all cases and bacteriologically in 100 per cent, the latter figure considerably exceeds the observations of the American investigators mentioned.

The authors join that group of investigators which holds that the streptococcus is the permanent inhabitant of the tonsils. The prevailing strain is *Streptococcus hemolyticus* (61.5 per cent). Second in order is the so-called *nonhemolytic streptococcus* (21.1 per cent). The *lactic acid streptococcus* figures in 10 per cent of the cases and the most infrequent is the *Streptococcus viridans* group (around 8 per cent). The authors stress the fact that the importance of the *microflora of the healthy tonsils* should not be underestimated or belittled and that infected tonsils should be removed.

A study based on cultures of nasopharyngeal swabbings taken once every 2 weeks for a period of almost 2 years was made by H. F. Helmholtz (Am J Dis Child 42:328 (Aug.) 1931) in a series of 18 children, aged from 2 to 14 years. Swabbings were taken in the homes of the children, great care being exercised to bend the wire applicator so as to avoid contact with any portion of the mouth and to touch only the nasopharynx. The swabs were taken to the laboratory immediately and rinsed in 2 cc of physiologic solution of sodium chloride, 2 drops were put in a Petri dish and incubated in 5 per cent blood agar. In the early part of the work inoculations were also made in deep tubes of dextrose-brain broth. These cultures were allowed to grow for 24 hours and then subcultures were made on blood agar.

As was to be expected, certain differences in the numbers of streptococci,

staphylococci and Gram-negative and Gram-positive bacilli were found, but since it was impossible by this method to show any relation to the original number of organisms, it was discontinued and only the direct inoculations of blood agar plates were used.

Of the total of 486 cultures, 216 (44 per cent) were positive for *Streptococcus hemolyticus* and 270 (56 per cent) were negative. In the 98 infections of the upper respiratory tract occurring in the special group during this period, positive cultures occurred in 49 and negative cultures in 49. It would appear that the mere presence of *Streptococcus hemolyticus* in cultures from the throat is of no significance. If, however, it represents a high percentage of the organisms present it may be of etiologic significance.

According to I. E. Pilot and I. Dreyer (J Infect Dis 49:135 (Aug.) 1931), *Streptococcus epidemicus* of epidemic septic sore throat produces a toxin, as determined by intradermal test, 98 of 324 persons (30 per cent) giving positive reactions. Susceptible persons, as well as rabbits, may be immunized with the *epidemicus* toxin. Skin reactions to the toxins of *Streptococcus epidemicus* are widely divergent from those to the toxin of *Streptococcus scarlatinae*. Of 208 persons, 46 gave positive reactions to scarlet fever toxin, 56 to the epidemicus toxin and only 10 to both toxins.

In about 50,000 tonsils examined by A. S. Warthin (Arch of Path 12:33 (July) 1931) during the past 35 years, 2 cases stood out as unique in that the tonsillar crypts contained spherical bodies having hyaline walls and packed full of spores, mostly in an unripe stage. The bodies varied from 30 to 300 microns in diameter. Larger, irregular,

partly collapsed or shrunken sporangia containing ripe spores were also present. The organism consisted of a spherical body with a definite but narrow hyaline, non-nucleated capsule, around which was a layer of thin, flattened, squamous epithelium derived from the epithelium of the crypt. This layer contained the nuclei mentioned by Taliaferro, was derived from the host, and was not part of the parasite. It was evident that the structure had developed within the mucosal epithelium. The hyaline capsule was thinner, less hyaline and chitinous than that of *Rhinosporidium seeberi* but was well defined. It stained pinkish with eosin. Within the capsule was a thickly crowded mass of unripe granular spores, staining bluish with hematoxylin. Only an occasional nucleus could be made out. Ripe spores and a finely granular material were noted in 2 collapsed sporangia. The structures were all embedded in the desquamated epithelium, which was heavily infiltrated with polymorphonuclear leukocytes and might have been termed a cryptic abscess. Beyond this, there was no evident reaction of the tonsillar tissues to the presence of the parasite. None was found in the lymphoid tissue or stroma. The process was purely a crypt infection. The author considered it important to record the unique observation in the tonsillar crypts of 2 of 50,000 tonsils, examined in his laboratory, of sporangia of an unknown parasite suggesting a close relationship with *Rhinosporidium seeberi*.

In a study of sporadic septic sore throat I. Pilot and D. J. Davis (J. A. M. A. 97:1691 (Dec 5) 1931) came to the following conclusions.

1 *Sporadic sore throat* most often is due to *hemolytic streptococci*, the streptococci in 10 per cent of the cases cor-

responded in their cultural characteristics to the *Streptococcus epidemicus* of epidemic septic sore throat.

2 *Septic sore throat* due to *Streptococcus epidemicus* in its usual form is sporadic. The epidemic type is unusual, requiring the development of a streptococcus mastitis in the cow whose milk becomes the source of the epidemic.

3 A *carrier state* for *Streptococcus epidemicus* may follow sporadic sore throat. Such carriers are probably responsible for the direct transmission of sore throat. The streptococci reside in the crypts of the tonsils, **tonsillectomy** is followed by their disappearance from the throat.

4 In its *clinical manifestation*, sporadic sore throat due to *Streptococcus epidemicus* varies from very mild to severe types. Patients devoid of tonsils may be affected and may give symptoms of an infection of the upper respiratory tract, in some ways resembling influenza.

5 *Complications* may arise immediately, such as otitis media, mastoiditis and cervical adenitis; sequelæ may develop from 10 to 30 or more days after the onset. Acute polyarthritis, endocarditis, glomerulonephritis and erythema nodosum were the most noteworthy and were often associated with mild recrudescence of sore throat and fever.

6 The *complications and sequelæ* were due to *Streptococcus epidemicus*. The appearance and disappearance of these organisms in the throat frequently could be demonstrated with the development and termination of the complications.

7 *Streptococcus epidemicus* constitutes probably a group among the hemolytic streptococci. Its capsule and large colony formation appears to be identified with an aggressiveness greater than

that of ordinary hemolytic streptococci and with a peculiar tendency to cause fatal peritonitis and meningitis. Its exact status remains unsettled

8. *Streptococcus epidemicus* produces toxin which gives skin reactions in man specifically different from toxin of streptococci of scarlet fever. Injected into animals, the toxin leads to the formation of an antiserum with neutralizing properties.

**ACUTE TONSILLITIS.**—From a study of acute tonsillitis and its sequelæ J. A. Glover and F. Griffith (Brit M J 2: 521 (Sept 19) 1931) believe that the following tentative suggestions are justified in view of all the available evidence:

1. Epidemic tonsillitis is one of the most common causes of invalidity in boarding schools and is due to infection with *hemolytic streptococci* of the *Streptococcus pyogenes* group

2. Infection of the throat with *hemolytic streptococci* produces varying clinical pictures in different persons. These include: (1) a symptomless infection, or healthy carrier state, (2) tonsillitis; (3) febricula, feverish catarrh or pharyngitis, without noticeable sore throat; (4) scarlet fever. Any of the latter 3 conditions may be followed by otitis media or by acute rheumatism.

3. Many serological types of *hemolytic streptococci* may cause scarlet fever, but certain types, the 4 "chief" types, predominate. Types 1, 2, 3 and 4 are together responsible for 70 per cent of the cases of scarlet fever admitted to fever hospitals in England, the remaining 30 per cent. being caused by strains forming a group of heterogeneous types.

4. Epidemic tonsillitis without rash is generally attributable to strains belonging to the heterogeneous group. These

strains cause scarlatina when their toxigenic powers are sufficiently high to overcome the antitoxic immunity of the person attacked

5. Observations made on 2 outbreaks of tonsillitis (only one of which has been described), attended with severe complications but without typical scarlatinal rashes, suggest that the 2 chief types concerned, types 1 and 2, may not invariably be of high toxigenicity

6. In any epidemic of scarlet fever, cases of tonsillitis and mild pharyngitis occur side by side with the cases of scarlet fever, and, if bacteriologic examination is made, numbers of healthy carriers will also be detected, all yielding the same type of hemolytic streptococcus as the scarlatinal cases. These unsuspected sources of infection constitute one of the most difficult problems in the control of scarlet fever.

7. Epidemics of tonsillitis in schools are generally associated with a high carrier rate of *hemolytic streptococci*

8. Epidemics of measles and influenza, even under the best of hygienic conditions, increase the spread of *hemolytic streptococci*, which are the chief cause of serious complications in these diseases

9. Often, however, epidemics of tonsillitis and high carrier rates of *hemolytic streptococci* are signs of the existence of environmental conditions which favor a rapid and easy transmission of infection. Chief of such conditions are too close proximity of beds, deficient floor area and deficient ventilation in dormitories.

10. Adequate spacing and ventilation of dormitories and classrooms, and proper intervals between beds in dormitories and school sanatoriums, are important factors in the prevention of the spread of infection.

B Exner and H Kotinetz describe the course of an epidemic in a home for nurslings (Jahrb f Kinderh 132.169 (July) 1931) Within 6 weeks, 40 children had sore throat and severe gastrointestinal disturbances *Hemolytic streptococci* were cultivated from the nasopharynx of the children and from the intestinal organs. A **polyvalent autovaccine**, prepared from the streptococci, together with **streptococcal serotherapy** gave favorable therapeutic results The port of entry of the hemolytic streptococci was probably the nasopharyngeal ring. This primary focus of infection led to a general sepsis, which was nearly always localized in the digestive and respiratory tracts.

A. Stroe, D. Hartopan and J Bazgan (Rev franç de pédiat 7 23, 1931) compare their results in 15 cases of *gangrenous tonsillitis* in scarlet fever with the observations of many other French writers and conclude with a favorable comment on the use of an **antigangrenous serum** in those cases Their experiences for the years 1928-1929 show that the proportion of mortality of cases encountered was over 75 per cent, while in 1930, with the extensive employment of antigangrenous polyvalent serum the mortality fell from 6 to 13 per cent The latter figure is for the complicated cases. It is well to remember that in 1930 there was in Roumania a most grave epidemic of scarlet fever.

**ACTINOMYCOSIS.**—F Allodi (Riforma méd. 47:254 (Feb. 16) 1931) reports an unusual case in a farmer, aged 30, who was working with a threshing machine, when it suddenly stopped He came near the machine to see what was wrong when suddenly the machine began to work again, blowing dusty particles of oats into his mouth Shortly after the accident the farmer

developed an acute attack of supposed diphtheria, which disappeared spontaneously after some days, leaving a chronic tonsillar actinomycosis with diminished ability to work When the patient was seen 4 years after the accident he had infected tonsils (which were removed), chronic pharyngitis and a fistula of long duration behind the right tonsil, which probably developed during the first acute attack. The case is considered under the point of view of industrial diseases which give workmen right to compensation The author states that in cases of this nature actinomycosis should be considered as any other infection with right to compensation and that, at the evaluation of the injury of the laborer, among late sequelæ of tonsillar actinomycosis the formation of abscess of the lung or of gangrene of the lungs, which may cause fatal complications, should be borne in mind.

**TONSILLECTOMY.**—Recent studies on the tonsil question bring the realization of a tremendous wave of enthusiasm tending toward the **electrodiathermic procedures** for the eradication of tonsils This method has perhaps had 10 years of experimentation and while the soil is fertile for further research along these lines, it has also opened up channels of promiscuous indications for commercial gain As yet, reliable scientific data is not available upon which indications can be better defined If the method warrants enthusiasm, then by all means it demands careful investigation to determine its value.

L. J Silvers (Arch Otolaryng 12 511 (Oct) 1930) reviewed his own experiences of some 6 years in this field He comes to the conclusion, in which he is joined by Skillern, that electrocoagu-

lation is an entirely safe and commendable procedure when complications contraindicate the usual surgical method. The method is not, however, wholly without danger, and certainly requires as much skill and knowledge as is required for surgical removal. For this reason Silvers urges the use of electro-surgical desiccation for young patients with *heart disease, tuberculosis* or *nephritis* and the occasional use of the **endothermic knife** for the freeing of the pillar or for other cutting procedures. There are other instances in which it is necessary to combine the use of the snare or dissection with electrical desiccation.

Among the *advantages* of electro-surgical methods he lists complete control of the operative procedure, accomplishment of the entire process of extirpation in any desired number of treatments, absence of shock and pain, prevention of hemorrhage, sterilization of the tonsils, and avoidance of anesthesia.

Among the *disadvantages* which he lists are the time required for safely controlled removal, and the time and effort required by the operator to master the technic.

Naturally, advocates of such a method bring to light statistics which tend to place in disrepute the surgical procedures but, suffice it to say, even a greater number of complications might occur with the electrosurgical methods were the results to be investigated. It can readily be seen that if tonsillectomy constitutes one-third of all the surgical operations done in America, a method much more accessible will have even a greater number of proponents, and its indiscriminate use will no doubt lead to many a mishap, by virtue of its supposed simplicity and apparent innocuousness. The argument is often advanced that it is the

method of choice when it comes to the physician's family or himself, but it is certain that those who know the timidity of the professional man simply ignore this particular point and brand it unscientific.

Many considerations must enter into the decision of the individual physician in the individual case as to whether or not electrocoagulation or surgical removal is to be the method of choice. Economically, surgical removal is less time-consuming and probably less expensive than electrical desiccation. It requires less frequent visits to the physician and by the physician. Apparently, in the hands of the unskilled, electrocoagulation may result in secondary sloughing and in abscesses much worse than those which rarely occur with surgical removal. Instances are on record in which the secondary complications have included such severe swelling and edema as to threaten the life of the patient. Some of those who have written on the subject urge that the method be employed only for adults, whereas other observers urge its value in young patients.

Electrosurgical removal of the tonsils cannot yet be considered established as the most desirable method for their routine removal. A competent operator, who has been thoroughly trained in the use of the method and who understands how to select his cases correctly, may get excellent results by its use. However, those who have not had special training of sufficient length may have unfortunate and, indeed, serious results with this technic.

Manufacturers of devices for this type of work have, with the usual commercial solicitude for disposing of the greatest amount of apparatus possible, offered 3-day courses to general prac-



tioners, who have then considered themselves competent to undertake electrosurgical removal of the tonsils. Unless they have a thorough understanding of the structure of the throat, of pathologic changes incident to removal of the tonsils, and of the possible complications associated with the electrosurgical method, the patients are likely to suffer. The unreasoning and unscientific promotion of this method not only by manufacturers, but by some writers on health subjects for the lay press, has done incalculable harm. In the vast majority of cases, electrosurgical removal of the tonsils has not yet been proved to be the method of choice. This should not interfere, however, with its application in properly selected instances. (J A M A Editorial 97 856 (Sept 19) 1931)

**Tonsillectomy in the Presence of Acute Infection.**—There is a tendency on the part of certain clinicians to get away from the orthodox principle of not operating in the presence of acute infections of the tonsils. In defiance of such principles S Levinger (Munchen med. Wchnschr. 77:1666 (Sept 26) 1930) performed tonsillectomies on 235 patients with *peritonsillar abscesses*. In 60 patients the operation was immediately preceded by a tonsillitis. He feels that when complications do occur, they are due to too radical operation at the lower pole of the tonsil. The author, like a number of American clinicians, believes that tonsillectomy is not only permissible during the existence of a peritonsillar abscess, but is the most favorable form of treatment, especially in cases of recurrent abscesses. So too, H. L. Baum (J A. M. A 95:1829 (Dec 13) 1930) defends the principle that it is not dangerous to remove tonsils at the height of an acute cervical adenitis. He defends

the performance of a surgical procedure which is contrary to preconceived opinion, recognizing the fact that the operation may frequently be done in such cases in as short a time as 2 weeks and even 10 days from the onset of the acute tonsillopharyngitis. Baum feels that his experience warrants the operation in *acute anterior cervical adenitis*.

**Deep Cervical Infections Following Tonsillectomy.**—A report of 30 cases and a review of the literature (80 cases) have formed the basis of an excellent anatomical and clinical investigation by S. L. Shapiro (Arch Otolaryn. 11.701 (June) 1930). The topographical anatomy is essentially that of the parapharyngeal space and its 2 divisions the prestyloid and retrostyloid compartments. The presence of the great vessels in this cavity, as well as its relationships to the base of the skull and neck, furnish a number of dangerous possibilities. In 94 per cent of all the cases reported by Shapiro the operation was done under local anesthesia, the most important factor being the injection of an infected solution into the parapharyngeal space. Clinically, 2 main types manifested themselves, *viz*, the phlegmonous and the vascular. The former was present in the majority of the cases accompanied by trismus, fever and swelling of the neck on the involved side, while the latter manifested itself as a septicemic thrombosis or embolism. The author advocates that the prophylaxis should consist of the avoidance of contamination of either the solution or the instruments and that the treatment should aim at localizing the infection before an attempt is made to drain the abscess. He advises that the incision be made through the tonsillar fossa, the external operation being indicated under certain conditions.

*End Results of Tonsillectomy.*—

The literature from year to year contains more investigations along the lines of end-results of the tonsil and adenoid operation. A. D. Kaiser (J. A. M. A. 95:837 (Sept. 20) 1930, Am. J. Dis. Child. 41:568 (Mar.) 1931) makes a comparative study of 2200 tonsillectomized children with an equal number of controls, 3 to 10 years after operation, and finds that

1. The real value of the operation cannot be determined in the first few years. The apparent benefits during the first few postoperative years are not so pronounced over a 10-year period.

2. Outstanding is the apparent influence on the incidence of sore throats over this period.

3. The child is rendered less susceptible to scarlet fever and diphtheria.

4. Acute head colds and otitis media, though lessened over a 3-year period, are not essentially influenced over a 10-year period.

5. Cervical adenitis is materially reduced.

6. The respiratory infections, such as bronchitis, laryngitis and pneumonia, occur more frequently in tonsillectomized children.

7. First attacks of rheumatic manifestations occur 30 to 50 per cent less often in tonsillectomized children, the greatest reduction being in the early operated cases. Recurrent attacks are not benefited at all.

8. Incomplete tonsillectomies do not offer the usual protection as do the completely done operations.

9. The hazards of tonsillectomy must be considered in evaluating end-results. Considering these, Kaiser finds that the late results seen in this group 10 years after operation are evident only in reduction of sore throat, cervical adenitis,

otitis media, scarlet fever, diphtheria, rheumatic fever and heart disease.

The operation, according to a study of 736 children before and after operation by J. D. Monroe and V. Volk (Am. J. Pub. Health 20:495 (May) 1930), offers the maximum benefit when performed early in childhood. Significant is the fact that complaints in their control group of cases did not show any improvement during the period of a year, whereas 91 per cent of improvement was shown by the group of patients operated on.

According to R. L. Cunningham (Arch. Int. Med. 47:513 (Apr.) 1931), one-third of 12,530 young white women who entered the University of California between 1920 and 1929 had had an operation for the removal of tonsils, one-third were thought to have normal tonsils, and the remaining third had pathologic tonsils, remnants of tonsils or buried or projecting tonsils to which no further designation was given. The group with normal tonsils and the group with pathologic tonsils differed by small percentages, which are statistically insignificant, in the incidence of the following diseases and operations reported in the histories: measles, mumps, chicken-pox, whooping cough, scarlet fever, diphtheria, pneumonia, pleurisy, chronic colds, rheumatism, chorea, operations for appendicitis, mastoiditis, enlarged cervical lymph nodes and operations on the nose.

The group with absent tonsils gave a history of higher incidence of all illnesses and operations than did either the group with normal tonsils or the group with pathologic tonsils. The fact that children who are often ill are the ones most frequently operated on is offered as a possible explanation for this higher incidence of illness.

The proportion of the amount of illness reported before and after tonsillectomy suggests that the removal of tonsils had little influence in lessening the susceptibility to most infections. The lack of proper comparative data lessens the value of this conclusion. The age when the tonsils were removed, had no influence on the total incidence of measles, mumps, chicken-pox, whooping cough, pneumonia and influenza, but early removal seemed to have a slightly favorable influence on the incidence of scarlet fever and, to a less extent, on that of diphtheria. The effect of the age of removal on chronic colds, rheumatism and otitis media was not conclusive.

A review of the literature relative to the effect of the condition of the tonsils on general health reveals a great lack of accurate information on the effect of tonsillectomy, when the number of operations that have been performed are considered. There is a growing tendency to question the value of tonsillectomy as a prophylaxis against infectious diseases and as a preventive measure or cure for such systemic diseases as rheumatism, chorea and carditis.

**Tonsillar Recurrences**, according to N Leshin and S J Pearlman (Arch. Otol 13 37 (Jan) 1931), are not entirely due to poor operative technic, but, based on embryologic and histologic studies, they found evidence that indicates that the *tunica propria* of the mucosa in this entire region contains lymphatic structures with marked tendency toward hypertrophy. The authors feel that the occurrence of hypertrophy in some instances and its absence in others is due to constitutional and individual factors as yet unknown.

**TORTICOLLIS, SPASMODIC.**  
See BASAL GANGLIA.

**TRACHEOTOMY, PERMANENT.** See LARYNX.

**TRACHOMA.** See CONJUNCTIVITIS, GRANULAR

**TRIBROMETHANOL.** See ANESTHESIA, BASAL: AVERTIN

**TUBERCULIN IN DERMATOLOGY.**—Tuberculin, whether ecto- or endo- tuberculin, is not poisonous for the nontuberculous organism.

The organism changed by tuberculous infection tries to change this poison into an innocuous substance.

An important factor in the foregoing conception is represented by the substances now generally called *procutines* and *anticutines*. J Jadassohn (Brit J Dermat 41 451 (Dec.) 1929) believes that the presence of procutines in the tissue of tuberculin papules, in the serum of tuberculin blisters, in the blood serum of patients suffering from certain tuberculous infections, and especially in the serum of animals very resistant to tuberculosis, is definitely proved. The anticutines are to be found in the serum of some tuberculous persons who have been treated with tuberculin, and also in certain forms of tuberculosis of the skin with specific anergy (the sarcoid group).

He has abandoned diagnostic subcutaneous injections for cutaneous reactions, favoring especially the Pirquet, the intracutaneous injections of Mendel, Mantou and the subepithelial injection of Takle. He has completely abandoned the ophthalmic reaction on account of damage to the eye. He considers the tuberculin ointment reaction of great importance. The demonstration of procutines and anticutines is sometimes used.

It is necessary to note late reactions, as the tuberculin reaction can develop

after an incubation period of several days

Jadassohn believes that tuberculosis, syphilis and leprosy have a tuberculoid structure in certain forms, in certain allergic periods, or in certain persons. Comment is made on the great difference existing between the accepted true tuberculids and conditions such as sarcoid, lupus pernio, lupus miliaris and granuloma annulare. The refractory behavior to tuberculin on the part of such a large percentage of patients with sarcoids and lupus pernio does not argue against, but is in favor of, a tuberculous etiology. The production of tuberculids may be considered as a local reaction to tuberculin, and that this has exhausted the local antibodies so that nothing has been left to react with the tuberculin introduced. A strong tuberculin reaction is a favorable sign and a weak or negative reaction, in tuberculosis clinically diagnosed, is considered to be unfavorable, representing as it does an existing anergy. Generally speaking, the lesions which react strongly to tuberculin are those conditions which are known to heal most rapidly.

Much uncertainty exists in prognosis based on tuberculin allergy. It is taken for granted in this article that the so-called tuberculids, strictly speaking, as well as the sarcoid pernio group are produced by the immediate effect of the bacillus on the skin. A problem exists as to the diversity of the tuberculodermas in spite of their identical etiology. Many factors may enter into this.

Accidental inoculation of young children resulting in severe ulcerating tuberculosis and auto-inoculation in adults suffering from severe internal tuberculosis are attributed to anergy. In the former case, the so-called normal antibodies do not yet exist; in the latter,

"cachectic anergy" is referred to. It is held that tuberculin allergy is important for the development of the special forms of tuberculodermas. It is important that cases be so treated that both the organism and the disease of the skin may be favorably influenced at the same time by the modification of the allergy.

**TUBERCULOSIS, PULMONARY.—VARIETIES.**—The medical literature on pulmonary tuberculosis in recent years is difficult to evaluate, due to the fact that the classification in use has no prognostic significance.

G. G. Ornstein, D. Ulmar and E. L. Dittler (Am Rev Tuberc 23 223 (Mar) 1931), recommending a new clinical classification of pulmonary tuberculosis, claim for their system that it will give some value to series of cases that are reported, and will enable the physician to determine intelligently the value of therapeutic measures, which they consider to be impossible at the present time. They suggest grouping cases under the heads of exudative, caseous-pneumonic, exudative-productive, and chronic proliferative. The classification does not include the primary infection with tubercle bacilli, but is reserved for cases of superinfection.

The authors assume that the altered reaction of body cells gives 1 of 2 responses, *i e*, either the *proliferative response* or the *allergic response*. The allergic response is held responsible for the exudative type of tuberculosis and the proliferative response for the other 3 types, these being modified to some extent by a lesser amount of allergic reaction. They further say: "For if an exudative and a caseous-pneumonic case can both be classified as far advanced, without any reference to their totally different pathological process, as is the

case now, how can one determine the result of any therapeutic measures? The exudative will recover regardless, the caseous-pneumonic will not. This simple error, engendered by our present classification, may serve to explain the different results obtained by different observers with the same therapeutic methods. Frequently cases are seen which combine 2 different types of pathological process, thus a person may have an apical caseous-pneumonic and a basal proliferative. It is only through a competent understanding of the underlying pathological process that one can intelligently classify the case. We believe our proposed modification of the existing classification supplies this urgent need."

**ALLERGY.**—A. Lumiere (Paris méd 1 393 (Apr 25) 1931) said that the allergic state consists of the acquisition, through humoral fluids, of a peculiarity of an anaphylactic type, conferred by the products of bacillary origin. This peculiarity causes those subjects once impregnated with these products to respond afterward to a second impregnation, which is not tolerated and tends to be expelled. This constitutional immunity is noted among infected persons, as well as in those subjects who have received only bacillary protein without living bacteria. If allergy is not always a sign of infection, it is significant of an anaphylactic condition and of resistance to a new inoculation. The predisposing power which is wrongly attributed to allergy leads to a state in which not enough distinction is made between allergy and infection. It is the infection which predisposes to new bacillary attacks.

L. S. T. Burrell ("Recent Advances in Pulmonary Tuberculosis," 2d Edit, Churchill, London, 1931) declares that there are 2 factors in regard to reaction

to reinfection (1) The natural reaction of the non-infected animal, which is proliferative and noninflammatory; (2) the acquired reaction peculiar to the previously infected animal, which is inflammatory. The tissues of such an animal are hypersensitive to tuberculin or tubercle bacilli and this condition of hypersensitiveness is spoken of as "allergy." In the case of a first infection, no symptoms of ill-health develop until the animal tissues become sensitive to the tuberculous infection, *i.e.*, until allergy appears.

Immunity is a function of allergy and it may be said of tuberculosis, as has been said of typhoid fever, that the beginning of symptoms marks the beginning of the immune period. Large doses of tuberculin which would be fatal to the allergic animal, cause no symptoms at all in the noninfected one, and the same applies to the injection of tubercle bacilli, except that after a latent period the bacilli will cause a general tuberculous infection. The latent or incubation period may, therefore, be regarded as the length of time taken by the body to establish immunity.

That immunity is a function of allergy may be shown by experiments. The allergic animal is made acutely ill by the injection of tubercle bacilli, but provided it recovers from the initial reaction, it will live much longer than one infected by a similar dose of bacilli for the first time, and in the nonimmune or non-infected animal allergy does not exist.

M. Pinner (Am Rev Tuberc 28:175 (Feb) 1931) is against this opinion. He believes that allergy and immunity quantitatively as terms are incomparable concepts. Immunity cannot be recognized or measured until the disease has run its course. It is not always true that a strong tuberculin reaction indi-

cates high immunity, nor is the reverse relation found to be true.

**ETIOLOGY.**—Tuberculosis in the aged is considered by J A Myers and H R Anderson (Am Rev Tuberc 21: 541 (Apr) 1930) one of the great problems from the standpoint of epidemiology Its danger lies in its mildness Many cases are not diagnosed until late in life and not a few are first diagnosed at the postmortem table

Recent indications in the literature on filtrates of tuberculous patients being capable of producing tuberculosis are contradicted by the experimental work of A. Larson (J Prev. Med 5 161 (Mar) 1931) Filtrates of sputum from tuberculous patients, containing numerous tubercle bacilli, were inoculated subcutaneously into 43 guinea-pigs, 10 receiving a Seitz filtrate, 22 a Berkefeld filtrate, and 11 a filtrate passed through both Seitz and Berkefeld filters. None of the animals developed the cachexia that is said to be characteristic of the more usual form of infection from filtrates, nor was there any enlargement of the inguinal lymph nodes at the point of inoculation. At necropsy, no lesions suggestive of tuberculosis were found Smears made from the tracheobronchial and retroperitoneal lumbar lymph nodes showed no acid-fast rods or granules Control guinea-pigs inoculated with small doses of unfiltered sputum from each patient died with generalized tuberculosis There is no evidence in these results that tuberculous infection is caused by Seitz or Berkefeld filtrates of sputum These observations are of importance and when considered in connection with the numerous negative results of others, make it probable that the positive observations that have been reported are due to some other factor than a filtrable virus.

**PATHOLOGY.**—Certain observers incline to the theory that tuberculosis is largely responsible for *calcified intra-thoracic exudates*, but there are others who hold that the cause is nontuberculous C C Anderson (Am J Roentgenol 22 531 (Dec) 1929) reports 3 cases favoring the claims of the latter group One was a case of interlobar pleurisy, the second a case of calcified exudate along the left ventricle of the heart, and the third a case of pericarditis calculosa This is the nineteenth recorded case of pericarditis calculosa diagnosed during life

**SYMPTOMS.**—J. A Myers and H R Anderson (Am Rev Tuberc 21: 541 (Apr) 1930) report that in 37 cases ranging in age from 50 to 80 years the duration of symptoms was from 6 weeks to approximately 45 years.

**COMPLICATIONS.**—C D Colby and K. Schaffle (South M. J 23: 801 (Sept) 1930) report 68 cases, in 43 of which both *hookworm disease* and tuberculosis were present, while there were 25 cases of *uncinariasis* which had been referred with a diagnosis of tuberculosis

According to E. M Jameson (Am. Rev Tuberc 22: 72 (July) 1930), tuberculous *pelvic disease* occurs in about 8 per cent. of women with pulmonary tuberculosis The diagnosis can be made with a reasonable degree of certainty on the history, symptoms, and observations on careful pelvic and abdominal examination The x-rays seem to offer a feasible, conservative method of treating tuberculous lesions of the uterus and adnexa in women with pulmonary tuberculosis In patients too sick for even this method of treatment, conservative treatment with **hot douches, baking and general medical measures** offers relief in a majority of



cases Surgery should be restricted to patients not relieved by other methods

On the basis of a review of the literature and his personal experience in 16 typical cases (the detailed clinical reports of which were published in his thesis), F. Condamin (Lyon chir 26 673 (Sept-Oct) 1929) points to the advantages of surgical treatment for such a condition. The extent of the intervention is dependent on the severity of the involvement. The author recognized 3 definite groups, of which the first is serous *salpingitis*. Absorption is noted under the influence of exposure to air, and laparotomy with insertion of a drain may suffice. In patients not exhibiting complications and without caseous or other lesions, salpingectomy or sterilization is superfluous. The *parenchymatous forms* of tuberculosis are usually complicated by intestinal adhesions; in this case partial resection of the *adnexa* is necessary although sterilization may be avoided and the lesions likewise tend to disappear after the operation. It is only in the last group of *caseous* and *suppurative tuberculosis* that a radical operation is indicated.

The incidence and the diagnostic difficulties in *genital tuberculosis* are discussed by F. Kermauner (Wien klin Wchnschr 43:1245 (Oct. 9) 1930). According to anatomists, tuberculosis represents from 1 to 2 per cent. of all genital disorders. For the clinician, however, the diagnosis is often difficult. Besides those cases in which tuberculosis is thought of, there are also cases in which there are no other complaints, as that of sterility. In other instances myoma and cancer are thought of, and only the operation or even the necropsy reveals the tuberculosis. During a period of 8 years the author observed 92

cases of genital tuberculosis. In a considerable number of cases, ascites was noted. In many instances the tuberculin test was made but it did not always prove reliable. In some cases the laparotomy insured the correct diagnosis.

In the surgical therapy of genital tuberculosis Hegar's method is still one of the most important. Some authorities advise against operative treatment. The author considers it necessary in some cases, particularly for diagnostic purposes; however, radical operation is, at least in younger patients, not advisable. In recent years the general treatment has been emphasized as the most valuable, especially dietary treatment, rest cures and fresh air and sunshine. Quartz lamp irradiation has been found helpful in *ascites* in young persons. In discussing x-ray treatment for genital tuberculosis, the author stresses that only small doses should be applied, in most cases about 10 per cent of a unit skin dose.

L. Michaux and G. Albot (Bull et mém. Soc. méd. d. hôp. de Paris 53:1262 (Nov 18) 1929) report the case of a patient aged 37 in whom tuberculosis of the *cervical lymph nodes* was noted in infancy. At irregular intervals of from 1 to 9 years, with disease periods of several years' duration, tuberculosis recurred in various forms. Among these may be mentioned *coxalgia*, *peritoneal symptoms* with *intestinal occlusion* and the formation of *bone abscesses* necessitating surgical intervention, as well as involvement of the left *kidney*. The patient recovered, however, 10 years after the last especially severe recrudescence of the disease and has since been able to follow a strenuous profession.

After a review of the literature, W. Iff (Schweiz med. Wchnschr. 61:244 (Mar. 14) 1931) is convinced that in

nearly all cases there exists simultaneously a generalized acute *miliary tuberculosis* or a miliary tuberculosis of the skin. The description of the microscopic structure of the tubercles of the *aorta* is also nearly the same in all reports. The bacillary content of the tubercle varies, but on the periphery it is usually considerable and occasionally also in the center. The descriptions of the microscopic structure of the tubercle vary in regard to the extension of the fibrinous and thrombotic stratifications, and also in regard to the depth of the foci and that some tubercles are only in the intima, while in other cases the media and adventitia are involved.

A necropsy was made on a cachectic woman, aged 70, who had died as the result of the following conditions: a recurrent endocarditis of the mitral and aortic valves, obliteration of the pericardium, a nodose, cavernous, pulmonary tuberculosis and lobar pneumonia of both lower lobes. The necropsy revealed the following. In the thoracic portion of the *aorta descendens* 3 miliary, caseated tubercles were found which contained an abundance of tubercle bacilli. Since the adventitia, media and also the deeper layers of the intima were free from tuberculous changes, the infection could have been caused only by way of the blood stream. It is surprising that, in spite of the ulcerated surface of the tubercles and the abundance of tubercle bacilli, a miliary tuberculosis did not develop. But since all the organs were not subjected to a microscopic examination, it is possible that the microscopic beginnings of a miliary tuberculosis may have been overlooked, or that a macroscopically recognizable miliary tuberculosis did not develop, because the patient died as the result of the lobar pneumonia and of the

general marasmus, before this could take place.

**DIAGNOSIS.**—Search for *tubercle bacilli in pleural effusions* has given heretofore such uncertain results that most microbiologists have become discouraged and have finally been inclined to admit that the fluid of these effusions exerts a lysing action on the bacillus. Karwacki, using ordinary culture mediums, succeeded in finding tubercle bacilli only 3 times, although he examined 33 liters of fluid. Schlossmann succeeded a little better by using the Petron method. F. Bezancon, in collaboration with his assistant, E. Buc (J. A. M. A. 97:1810 (Dec 12) 1931) is reported to have recently solved the problem. He observed that the pleural fluid immediately modified its hydrogen ion concentration through loss of carbon dioxide. It is, therefore, necessary to acidify slightly the culture medium. The medium he uses is composed of distilled water, to which is added 2 per cent of peptone, 5 per cent of glycerine, and 1 per cent of monobasic potassium phosphate and sodium phosphate. Several tubes are filled with from 2 to 3 cm in height and a few filaments of cotton are added. The contents are sterilized at a temperature of from 110° to 115° C, and an equal quantity of pleural fluid is added. The tubes are well stoppered and are kept in a bath at an exact temperature (between 37° and 38° C). The colonies appear in from 3 to 4 weeks, either on the threads of cotton, which were added to serve as their support, or at the bottom of the tube. They increase in volume in the form of arborescent prolongations, especially in the more aerated region of the surface. The bacilli appear in countless numbers, and present their usual characters as to form, acido-resistance,

and inoculability in the guinea-pig. The positive results are virtually constant, especially if the pleural exudates of artificial pneumothorax are considered

II C Sweany and A Stadnichenko (Am Rev Tuberc 22 420 (Oct) 1930) reported the results of 106,464 *sputum examinations* by the *incubation concentration method*, of which 16,103 were positive. Fifteen per cent more positives were obtained by concentration than by direct smear in a control series of 1500 specimens. No false positives were obtained in 6283 examinations on negative controls consisting of observation cases, nontuberculous diseases, and closed tuberculosis. Sixteen positive diagnoses were justifiably questioned, because they did not conform to the clinical and x-ray observations at the time of the sputum examination. Of the 16, 6 were proved to be tuberculous, 6 were probably tuberculous, 1 was probably not tuberculous, there was 1 in which the bacilli were avirulent or indifferent, while 3 were probably errors in technic. This virtually leaves 4 errors in 16,103 positives, or 1 in about 4000. From this work the authors believe that atypical acid-fast forms, when found alone, should be considered only suspicious until proved otherwise. There appear to be no more sources of error with this method than there are with any other method of similar technical manipulation.

G Ninni (Ann de l'Inst. Pasteur 45 433 (Oct.) 1930) *injected* directly into the lymph nodes of guinea-pigs various material suspected of containing tubercle bacilli: pleural fluids, cerebrospinal fluids in meningitis, pneumonic exudates, pus from suppurative adenitis, purulent feces of enteritis, etc. Three guinea-pigs were inoculated with each substance; 2 were inoculated into the

lymph nodes with 0.1 cc and 1 subcutaneously with 2 cc

The inoculations of pleural and cerebrospinal fluids were usually followed by the development of tubercle bacilli in the lymph nodes within 8 days, the other substances required 12 days. This is a much shorter time, however, than is required with the method of subcutaneous injection. The guinea-pigs were kept alive for some time after the ablation of the inoculated lymph nodes; all those in which tubercle bacilli had been found presented clinical symptoms of tuberculosis. When the substances injected contained other bacteria also, there was no effect on the lymph node and was not evident after 8 or 12 days; this is a distinct advantage over the subcutaneous injections, in which the bacilli always produce an abscess at the point of inoculation. The great saving of time, as well as the specificity of the method, resulting from the elimination of the associated bacteria, leads the author to consider inoculation directly into the lymph nodes a valuable method of diagnosis of tuberculosis.

In a series of 300 cases of urogenital tuberculosis, T von Huth and F. Lieberthal (Surg. Gynec. Obst. 50 985 (June) 1930) used the *Loewenstein-Sumyoshi method* of culturing tubercle bacilli from urine on the culture medium of Lubenau modified by Hohn, and it proved itself not only more convenient but more accurate than any previously employed method for the *determination of Koch bacilli in the urine*. The cultures have been grown on the Hohn egg medium as well as on the glycerin potato.

E. Loewenstein (Munchen med Wchnschr. 78.261 (Feb 13) 1931) directs attention to his culture method (*Ibid.* 77:1662 (Sept 26) 1930) which

makes it possible to detect *tubercle bacilli in the blood stream*. The author stresses the advantages which his method has over other diagnostic methods. In 5 patients in whom a slight increase in temperature existed, but in whom neither physical nor x-ray examination revealed a pulmonary focus, tubercle bacillemia was discovered with the author's culture method, and the further course of these cases proved that the diagnosis of tuberculosis had been correct. In cases showing progressing anatomic changes the proportion of positive reactions obtained with the culture method were about 80 per cent. Tests on blood specimens were made without knowledge of the diagnosis and it was found that in gonorrhea, syphilis, psoriasis, and carcinoma the culture method always gave negative results.

In metastatic forms of tuberculosis, especially in tuberculosis of the skin, the blood culture test was positive as long as the process was acute, in tuberculosis of the genital tract the same condition was observed. The positive results in acute and subacute polyarthritis were so numerous that they cannot be considered accidental. The author discovered tubercle bacilli also in the blood of a patient with spinal meningitis and in several other patients with disturbances of the central nervous system. However, as yet, no general conclusions have been reached with regard to the occurrence of tubercle bacilli in diseases of the central nervous system. The author comes to the conclusion that the blood culture method is more reliable than either the examination of the sputum or the tuberculin test, and because of its diagnostic and prognostic value, he recommends its general application.

In the *differential quantitative tuberculin test*, J. E. Blair and W. I. Galland (Am. Rev. Tuberc. 23:1 (Jan.) 1931) use potent human and bovine tuberculin in parallel series. The dilutions used are so chosen that the basic dilution is of a potency comparable to that of the Mantoux test, and the series extends to dilutions sufficiently weak to exclude all but the truly hypersensitive tuberculin reactors. These dilutions, with tuberculin of a potency usually found in commercial samples, range from 1:10,000 to 1:10,000,000. Inclusion of both human and bovine tuberculin diminishes the possibility of missing occasional cases, which might be overlooked when only 1 type of tuberculin is used. A total of 471 cases is reported, comprising children and adults, tuberculous and nontuberculous. Of 121 tuberculous cases, 90.9 per cent reacted positively to the diagnostic dilutions, and 9 per cent gave a negative reaction. Of 350 nontuberculous cases, 92.5 per cent gave a diagnostically significant negative reaction and 7.4 per cent reacted to the diagnostic dilutions. Of 23 tuberculous cases tested with both human and bovine tuberculin, 4 (17.3 per cent) would have been missed had only 1 type of tuberculin been used.

Reporting a case of pulmonary tuberculosis, proved at autopsy, C. J. Bucher (J. A. M. A. 90:1289 (Apr. 21) 1928) states that the repeated negative *von Pirquet reactions* are difficult to explain when it is considered that 5 tests were performed by 5 competent observers with different samples of tuberculin. Unquestionably, the tests served only to obscure the diagnosis in this case. Like many other tests used in clinical medicine, repeated negative von Pirquet tests do not necessarily rule out an extensive active tuberculosis.

*Pittings or depressions in the finger nails* were observed by A. G. Hahn (Am Rev Tuberc 20 876 (Dec) 1929) in 100 per cent. in a group of patients suffering from active pulmonary tuberculosis, as compared with 6 per cent of a group of patients who had been inactive for a relatively short period, and a third group of inactive cases (without symptoms of activity for from 1 to 25 years) in whom this change was found to be absent in 100 per cent. of the cases studied. In the opinion of the authors, therefore, the occurrence of these characteristic pittings in a known case of pulmonary tuberculosis should be regarded as indicative of recently active tuberculosis, provided no other disease is present.

*Hippocratic incurvation* was found in 76 per cent of the active tuberculosis group, 50 per cent of the inactive tuberculous group, and 30 per cent of the ex-patient workers at the sanatorium. This change did not occur in any of the non-tuberculous controls (presumably normal individuals).

*Cyanosis of the nails* was noted in 66 per cent of the active group as against 2 per cent of the inactive or chronic group. This change was well marked in all cases in which the disease was rapidly advancing, as evidenced by clinical symptoms and x-ray studies. From these observations it is believed that cyanosis may be of value in prognosis.

*Ridging* seems to be of less importance than the other changes described.

**PROGNOSIS.**—F. M. Pottenger (Ann. Int. Med 4 281 (Sept) 1930) concludes that tuberculosis heals as a result of the patient's immunity reaction. The efficiency of this immunity reaction is increased by repeated reinoculations. The effects of immunity are shown in the following services rendered

the host: (a) destruction of bacilli; (b) retardation of the passage of bacilli through the tissues, (c) elimination of bacilli through natural channels by caseation and cavity formation; (d) development of a state of sensitization to bacillary and nonbacillary toxins; (e) encapsulation or rendering inactive viable bacilli which remain in the tissues, (f) ridding the body of the inflammatory products that accompany infection, and (g) repair of the injury inflicted on the body by the disease. Treatment is efficacious to the extent that it is able to limit reinoculations of bacilli and bacillary protein to a minimum and create within the patient a resistance capable of coping with them as they occur.

L. H. Fales and E. A. Beaudet (Am Rev Tuberc 23 690 (June) 1931) do not agree with the authorities who believe that the tuberculous cavity is the death sentence of the bearer. In their investigations they found that a surprisingly large percentage of cavities healed. They found, however, that the capacity of cavities to heal depended greatly on 2 factors: (1) the size of the cavity, and (2) the amount of the pulmonary involvement. They believe that the rest treatment is of greater importance in the healing of cavities than artificial pneumothorax, thoracoplasty, or other surgical measures. In the average cavity case, which is not definitely retrogressive, and is without elevation of temperature, rest should be the treatment selected for at least 12 or 18 months. Then if the cavity does not show a tendency to heal, pneumothorax or other surgical procedures should be resorted to in suitable cases. In bilateral cavitation, the prognosis is not good.

In order to attain the best results, rest must be prolonged, continuous and with-

out interruption. Patients with cavitation should rest from 20 to 24 hours each day. In the authors' series it was found that, when the treatment was interrupted, 30 per cent of the cavities healed, whereas when the hospitalization was continuous, 41 per cent healed.

**PROPHYLAXIS.**—The numerous avenues open to the tubercle bacillus by which it may reach new hosts make any practical suggestion for closing any of these of great interest. Kopeloff and Davidoff (Proc Soc Exper Biol and Med 28:7, 1930) found that **chlorine gas in tap water** in a concentration of 30 to 50 parts per 1,000,000 is an active disinfectant, and rendered suspensions of tubercle bacilli in water noninfective for guinea-pigs in 5 minutes. They suggest the possible application of this in restaurants, soda fountains, drinking places, etc., where contamination with tubercle bacilli is encountered.

J. Heimbeck (Presse méd 37 1391 (Oct 26) 1929) writes that for a considerable time it has been the practice at the Ulleval Hospital, Oslo, to vaccinate student nurses who present a negative von Pirquet reaction by *subcutaneous injection of B. C. G.* The reason is that, if not vaccinated, these nurses are apt to develop more or less serious tuberculous lesions shortly after they begin to work in the wards devoted to tuberculous patients, whereas nurses reacting positively to the von Pirquet test escape the infection entirely or develop only benign lesions. He has found that injections of the Calmette-Guerin bacillus provoke a positive tuberculin reaction within about 2 months.

Of 34 nurses who were not vaccinated, 14 developed more or less serious tuberculous lesions, whereas of 136 vaccinated nurses who were serving on identical services, only 3 became infected

and these developed only slight signs of pleurisy.

In reporting an investigation carried on since 1926 in Norway, which included country dwellers, the 2 classes of townsfolk, the middle class and the workers; subjects of all ages, presumably healthy, J. Heimbeck (Arch Int Med 47 901 (June) 1931) made the following conclusive statement: "Tuberculous infection occurs in the minority of persons during childhood (the first period of infection), and in the majority during adult life (the second period of infection)."

"Tuberculous diseases are generally the direct result of a newly acquired infection. An infection that does not presently reveal its malignancy with symptoms of disease, but merely causes allergy, will seldom give rise to disease processes later, on the contrary, it protects the organism against any new exogenous infection. Pirquet's tuberculin reaction in a healthy person is, therefore, to be regarded as a sign of immunity. Subcutaneous vaccination with B. C. G. is harmless, and, as a rule, produces immunity, often associated with allergy. The immunity is equivalent to a benign tuberculous infection, but is probably not permanent. As within a certain time, perhaps from 1 to 4 years after the vaccination, it seems to be strengthened and stabilized by any later tuberculous infection, those vaccinated possibly ought to be infected with tubercle bacilli or revaccinated with B. C. G. the first year or 2 after vaccination. In persons in tuberculous surroundings and giving a negative von Pirquet reaction, *subcutaneous vaccination with B. C. G.* is the sovereign means of preventing tuberculosis."

The use of **Langer vaccine**, made of young virulent bacilli, killed by heat, for



immunizing purposes, is strongly recommended by D P Brachman (Am Rev Tuberc 22 226 (Aug) 1930) There is no apparent risk, present or future, connected with its application, and results in Europe are entirely in its favor It is necessary, in order to procure the largest number of subjects for this vaccination, that tuberculosis be diagnosed early, resulting in contacts having the least amount of exposure, and hence less likely to become infected Also, there must be sufficient institutional beds so that tuberculosis patients can be immediately hospitalized, again limiting the length of exposure of contacts Failing the latter facilities, additional quarters for the young contacts pending testing and vaccination would suffice, but the parents' consent to this arrangement is not forthcoming in the great majority of cases

**Immunity and Tuberculosis.**—While E Hedvall (Hygiea 93·113 (Feb 28) 1931) established bactericidal substances active against tuberculosis in the blood serum, these substances do not, in his opinion, play an important part in causing immunity to tuberculosis. The author inclines more to the theory that immunization against tuberculosis depends on a physiochemical change in the cells which decreases their susceptibility to tubercle bacilli, and advises a closer study of this change in the cells of the organism after a tuberculous infection

E Hedvall (Ztschr f Tuberk 60·97-176 (Apr) 1931) believes the existence of immunity against tuberculosis is now admitted by most investigators; however, knowledge of the nature of this immunity is still incomplete. It was possible for the author to demonstrate in the serum and in the plasma the occurrence of bactericidal substances

which are effective against tubercle bacilli, but he questions that these bacteriolysins have an essential significance for tuberculosis immunity He asserts that the results of his investigations are such as to create doubts in regard to the usual explanations for immunity against tuberculosis According to most of these generally accepted theories, immunity against tuberculosis is due to an increase in the bactericidal capacity of the body fluids or cells However, the author considers as more reasonable the theory that immunity is due to changes in the cells, by which their susceptibility to tubercle bacilli is reduced Because of this decreased susceptibility of the cells, the tubercle bacilli, so far as they are not dissolved by nonspecific ferments or are not excreted by the kidneys or the intestines, may remain in the tissues without causing tuberculous changes However, the tissues may lose their increased resistance to tubercle bacilli through such influences as serious diseases, pregnancy, or starvation, and then the bacilli may form new tuberculous foci

**TREATMENT.**—M J Breuer (Ann Int Med 4 1447 (May) 1931) states that the effect of **tuberculin** is to decrease the patient's allergic sensitization Its effect in increasing immunity is negligible Clinically, it ought to be useful in those cases in which the allergic state is principally at the basis of the patient's symptomatology A series of 26 previously unresponsive cases selected for treatment with this distinction in view, showed no contradiction and probably confirmation of the above idea Analysis of 181 unselected cases previously treated, also confirms the idea

In discussing the treatment of *mixed infections* in patients with pulmonary

tuberculosis, Veilchenblau (Munchen med. Wchnschr 76:2165 (Dec 27) 1929) points out that the temperature in patients with tuberculosis is often not in proportion to the severity of the tuberculous process. Patients in whom the tuberculosis is of a mild degree often have a higher temperature than those in whom the tuberculous process is further advanced. The author assumes that this is due to infections with other pathogenic organisms, and he also thinks that these infections increase the virulence of the tubercle bacillus. Consequently, he hopes to decrease the severity of the tuberculous process by counteracting the mixed infection. The sputums of 58 patients with tuberculosis were examined and in most cases a mixed bacterial flora was found. **Autogenous vaccines** were prepared and with these the patients were given repeated injections. The treatments were given at intervals of 3 days. In the first injection 0.2 c.c. was administered. This quantity was gradually increased to 0.12 c.c. The result of the treatment was that the temperature decreased considerably, the quantity of sputum became less, and the general condition improved. Complete cure of the tuberculous process could not be effected. However, if the general condition is improved, the organism has a greater resistance against the tubercle bacillus.

B. Gordon and A. Cantarow (Am Rev. Tuberc 20:901 (Dec) 1929) made an x-ray study of 60 tuberculosis patients to whom **parathyroid extract** was administered (10 units twice daily) from 1 to 4 months. No specific change was shown in the course of the disease except as obtained through the relief of signs and symptoms, notably hemoptysis, pleurisy, cough, and expectoration.

There was no evidence of decalcification or increased calcium deposition in the lungs. **Parathyroid extract** (20 units every 48 hours) and **calcium lactate** (30 grains—2 Gm—3 times daily) were administered to 14 patients with pulmonary tuberculosis for a period of from 1 to 6 months. The results were similar to those noted in the first group. X-ray studies failed to reveal any change in calcification of lung fields or bones of the hands, and there was no visualization of the blood-vessels.

It appears that diseased or potentially diseased tuberculous tissue is not influenced directly by hypercalcemia and that parathyroid hormone and calcium should not be administered with the expectation of inducing calcification. The influence of these agents on certain phenomena arising during the course of the disease may be considered of value in treatment.

**Dietary.**—There have been many special diets for tuberculosis, none of which, however, have stood the test of time. The one which is being most discussed at the present time is the **salt-free diet**. Opinions as to its value are flatly contradictory. Most authorities concede its value in tuberculosis of the skin.

M. G. Schroder (J State Med 39:435 (Aug) 1931) believes that in most cases of chronic tuberculosis in the human subject a **mixed diet** with plenty of proteins and fats is indicated, containing sufficient salts and vitamins and insuring a moderate hypernutrition. The cases cannot be treated rigidly by rule, but the whole personality of the patient must be taken into account. There is no special curative diet for tuberculous troubles. Special diets may sometimes be useful to tone up the system, and, in the presence of disturbances of important organs, may bring

about symptomatic improvement. It is necessary, therefore, to attend strictly to the indications present and to individualize.

The value of the dietetic treatment of Gerson, Sauerbruch, and Herrmannsdorfer rests on its stimulating effect. While useful for some cases of tuberculosis of the lungs and mucous membranes, but harmful to others, the mode of action has not been unequivocally proved; it probably depends on removal of table salt. It is only generally useful in forms of skin tuberculosis and in some cases of bone and joint tuberculosis. The number of questions raised by it is, however, so complicated that a long course of clinical and laboratory investigation will be needed to clear the matter up; from his own observations, however, the author believes that care must be exercised in employing this new therapeutic method which has little symptomatic value.

Attention is called by P. Wichmann (Beitr. z. Klin. d. Tuberk. 75:100 (Sept. 17) 1930) to the fact that a form of therapy that has a favorable influence on external tuberculosis is not necessarily of value in the internal form. He has seen cases in which dietary treatment resulted in the healing of tuberculosis of the skin, but was followed by the appearance of a fresh tuberculosis of the internal organs or by the exacerbation of an already existing internal tuberculosis.

The advantages of carbohydrates as food, *viz.*, their rapid resorption, slight or absent dynamic action, protein conservation, and an improvement in the assimilation of fats, are emphasized by E. Grafe (Beit. z. Klin. d. Tuberk. 75:42 (Sept. 17) 1930). Contrary to the view of Chlebnikow and Gerson and Herrmannsdorfer, he believes that the

increased carbohydrate requirement of tuberculous patients should not be ignored and that they should be given carbohydrates in large amounts. They should constitute the chief source of calories in the diet.

M. J. Breuer (Am. Rev. Tuberc. 22:57 (July) 1930) states: "The Munich diet, which attracted attention for a while, served to emphasize one new point, *ie.*, the usefulness of a low-salt diet. Modern civilized diet contains far too much sodium chloride. According to Ostwald's law of the mass action of the concentration of ionized salts in a chemical reaction, an excess of one salt, such as sodium chloride, will decrease the effective concentrations of the other salts, such as those of calcium, potassium, magnesium, etc., to the point of actual deficiency." The author considers that calcium is especially necessary to recovery in tuberculosis cases; there may actually be a calcium deficiency for no other reason than excessive indulgence in sodium chloride. For *a priori* reasons, the author states that he cannot help considering the restriction of sodium chloride a tremendously important nutritional factor in this treatment.

**High Altitudes.**—Thirty years of work with lung diseases has served to strengthen more and more the conviction of O. Amrein (Beitr. M. J. 2:1188 (Dec. 28) 1929) of the superiority of treatment at high altitudes. The statistics of the so-called immediate results after a course of treatment at Arosa, Switzerland (altitude 5900 feet above sea level) worked out from data in 4000 cases, show that in stage I cases there were 93 per cent. of positive cures, in stage II cases, 74 per cent.; and in stage III cases, 41 per cent. Statistics of the more permanent results

7, 10, or more years after the cessation of treatment, show that permanent results were obtained in 86.5 per cent. of stage I cases, in 12 per cent of stage II cases; and in 7.5 per cent of stage III cases.

At the beginning of their treatment at Arosa, 83.6 per cent of the patients with a durable result were afebrile, and 82 per cent had a pulse rate below 100. In 40.86 per cent of all patients there were still some physical signs but no evidence of activity from 1 to 9 years after treatment. The sputum still contained bacilli in 3.8 per cent; 18 per cent had some active trouble, and continued under treatment.

The best results were obtained with patients between the ages of 20 and 30 years (51.9 per cent of durable results), and with patients who started treatment within 6 months after the first symptoms were observed. Taking all stages together, 63 per cent of all the patients were still fully fit for work from 1 to 9 years after having stopped the treatment.

**Heliotherapy.**—According to E. H. Bruns (Mil Surg 66:1 (Jan) 1930), the care of tuberculous soldiers as established by Colonel Bushnell more than 20 years ago has undergone few changes. No specific treatment has ever been used; no fads or any of the much exploited so-called cures have ever been introduced. It has not been a treatment by drugs or serums aimed at the direct destruction of the tubercle bacilli but an effort to restore the failing resistance of the body by rest, open-air, and nourishing food. It has withstood the test of time.

S. H. Watson (Arch Physical Therap 10:252 (June) 1929) considers that heliotherapy is by no means indicated in all cases of tuberculosis. There

are many tuberculous patients who should never use it. In general, direct sunlight is indicated in cases of extrapulmonary tuberculosis and contraindicated in cases of pulmonary tuberculosis. For no type of tuberculosis is heliotherapy a cure, but often, especially in the extrapulmonary cases, it is a very valuable, or even necessary, aid. Since it is not in itself a cure, heliotherapy should never be used to the exclusion of the usual standard therapeutic measures. Never should it be forgotten that the direct rays of the sun are extremely powerful, and that, carelessly administered, they can effect great harm. Direct sunlight, in the same amount, affects patients differently—more differently, especially, in the beginning of its use, than almost any other remedy. Obviously, therefore, it must be used, in every case, not according to any hard and fast rule, not according to any theoretically predetermined dosage, but according to the individual reaction. Heliotherapy is of the greatest value, and may be practiced with the least chance of doing harm, in pure extrapulmonary tuberculosis, *viz.*, in the so-called surgical tuberculosis without pulmonary lesion. It is of great value in extrapulmonary tuberculosis with coincident pulmonary lesion; but in its use in these cases far more care must be exercised than in the uncomplicated surgical type, particularly as regards exposing the thorax. It is of great value in hilar gland tuberculosis, and in this type should invariably be used. It is of some value in some cases of the proliferative type of pulmonary tuberculosis; but here it must be employed with the greatest caution, lest it transform a favorable, stationary, or healing lesion into a rapidly progressing and fatal one. It is virtually never of value, and is

often positively harmful, in the exudative type of pure pulmonary tuberculosis, as well as in all acute types; in such cases, therefore, it should never be used

### **SURGICAL TREATMENT.—**

The employment of surgical measures, in addition to general rest, dietetic regimen and phototherapy is receiving more attention. Opportunity for the presentation of large series of cases has come in many clinics, making possible comparative studies of groups of similar size and pathologic classifications which have and have not had surgical therapy in addition to hospital or standardized care. The physician is better able to determine the relative values of various technical procedures in this way, rather than by consideration of statistics compiled from numerous nonrelated sources. Where a series of considerable size is reported from a single clinic, it is taken for granted, unless definitely stated to the contrary, that the requirements for surgical acceptance have been uniform throughout the series; and the statistics of ultimate end results, therefore, possess a more definite value than compilations where such requirements for surgical acceptance vary greatly, and uniformity in surgical technic is lacking.

Surgical therapy, as applied in the treatment of pulmonary tuberculosis in the large majority of cases is, in the last analysis, but a different measure for obtaining the mechanical and physiologic rest, recognized as a necessity in the treatment of tuberculosis wherever found. Justification for its trial existed in the promise that it provided a means for securing this rest more promptly, directly and completely and, in certain instances, over rather sharply circumscribed areas. To be continued as accepted methods in the treatment of pul-

monary tuberculosis, surgical procedures must demonstrate in late follow-up studies, that the heretofore prolonged rest period can be materially shortened, giving them an economic value on one hand, and at the same time must demonstrate that the percentage and permanence of favorable results are as great or greater than those of the medical measures hitherto used.

The proponents of surgery believe they are now able to demonstrate the value of surgical interference in selected groups of cases, both from the standpoint of economic value during treatment, and from that of increase in percentage of favorable results obtained.

To obtain physiologic rest for a lung the seat of tuberculosis, one of 2 fundamentally different methods must be employed. One method seeks to limit the expansion of the lung within the little disturbed framework of the thoracic cage. This may be by introduction of gas or oil, where a general compression is desired, or by local compression with paraffin, special plastic preparations, or living tissue, as when pectoral muscle has been employed, in lesions limited to fractions of the upper lobes. The other method seeks to limit pulmonary expansion by immobilization of some part or all of one-half the costal cage, and with a great reduction in the capacity of the hemithorax.

Occasionally circumstances of pathology are such that a deliberately planned combination of the above methods may be used, or sequelæ may develop which render a combination desirable or even necessary.

The operations to secure partial immobility and reduction in cubic content of the hemithorax vary much in extent and severity. They may involve but slight risk, as in operations upon the

phrenic nerve, or in the multiple resection of the intercostal nerves; or they may be much more formidable, as in a thoracoplasty, where most careful selection of the type of case must first be made and then as much consideration given to the question of anesthesia, to the division of procedure into stages, and to the intervals between the stages.

Limitation of expansion within the little altered thoracic cage has its greatest application in the introduction of air or nitrogen into the pleural cavity to produce compression of the involved lung.

**Pneumothorax.**—After years of extensive experience the value of this method of securing lung rest is assured. The question of its employment is dependent on 2 factors that concern the patient. One of these centers about the type of the pathologic process, whether the subject, when coming under competent medical care, has or has not extensive pleural adhesions, as well as the intrapulmonary pathology. The other question involves the economic side. Is it financially available? Experience has taught that lung rest secured by this method must, like rest in tuberculosis elsewhere, be continued over a period of several years, with regular checking of local conditions and refillings, to maintain what has been determined to be the individual patient's optimum intrapleural pressure. In other than metropolitan districts, or in sanatoria, where the patient cannot be in close contact with the physician competent to do this work, a drawback is thus offered. Where, especially in metropolitan districts, it can be employed, its economic value is stressed by reason of the patient's possible earlier return to partial employment at least. A similar shorter hospitalization time is recognized as giving

it added value in potentially increasing the bed capacity of the institutions.

**Indications.**—The patients considered suitable for this type of surgical therapy are listed by A. J. Cohen (Pennsylvania M. J. 32:862 (Sept.) 1929) as follows: "I believe all cases of *acute* or *subacute exudative pulmonary tuberculosis*, with considerable toxemia and a progressive lesion with or without cavity formation, should be treated by artificial pneumothorax. A large experience has convinced me that we have been too conservative and that we are not resorting to this treatment early or often enough. Astoundingly quick results are obtained in cases of acute illness with a rapidly progressive moist lesion, or with a persistent and profuse hemoptysis associated with high fever, and with that unpleasant symptom-complex which constitutes intense toxemia. The operation is indicated in every case of moderately advanced tuberculosis in which the disease has not yet affected the contralateral lung and there is still a free pleural space. Active disease in the contralateral lung, or massive adhesions on the diseased side render the operation ineffectual in the former and impossible in the latter. It is not indicated in the minimal stage of the disease, it is not good in chronic fibroid phthisis; it is useless in far advanced dying consumptives; *but I claim there has been a day in the life of every far advanced and hopeless case when an artificial pneumothorax could have arrested the progressive process, prevented the spread of the disease to other organs, and saved the individual's life.*"

J. D. Macfie and G. Napier (Brit. M. J. 1:442 (Mar. 8) 1930) consider that possibly, on the whole, there is too much delay before inducing a pneumothorax. Harms and Grunewald (Beitr.



z. klin d Tuberk 76 201 (Dec 22) 1931) state that artificial pneumothorax is absolutely indicated in cases of *unilateral fibrous* or *fibrocavernous tuberculosis*, also in cases of *unilateral chronic infiltration*, and in cases of *early unilateral infiltrate*. They speak of the indication as being urgent in *severe hemoptysis*, their conclusions being based on a series of 800 cases

A slowly increasing number of favorable reports is accumulating in which pneumothorax therapy limitations have not been so sharply drawn, and it has been used in recognized cases of involvement of the contralateral lung, experience having indicated that reduction in general toxemia by treatment of the more involved side enabled the reparative process to deal successfully with an early process in the contralateral lung A Baer (Beitr z klinik d. Tuberk. 72 290 (July 15) 1929 )

But beyond this extension of the line to such cases, others have gone to the extent of bilateral induction S Bader (Ztschr f Tuberk 61·209 (July) 1931) reports a case in which *bilateral pneumothorax* was maintained for 2½ years E R Schauman (Nord. Tuberk laegefor. Forh p. 73, 1930) reports on 14 cases P. F Armand-Delille (Medicine 12·333 (May) 1931) reports on 22 cases—and concludes that even in such type a cure can be looked for in a third of the cases I D Bronfin (Am Rev Tuberc 23 661 (June) 1931) concludes that many patients who develop contralateral disease during the course of pneumothorax therapy, or who have bilateral disease equally distributed, can be treated successfully by means of alternating pneumothorax, and that in some instances a complete arrest may be accomplished. L. J. Moorman (South M J. 23:1088

(Dec ) 1930), after reviewing the reported work of at least 20 operators, involving more than 100 treated cases, states that he is impressed with the unanimous agreement in the efficacy of this method of treatment It is admitted that arrival at a just decision for induction of *bilateral pneumothorax* is difficult, and "in discussing the indications for bilateral pneumothorax in the light of personal experience the writer states that it seems only logical to study each lung thoroughly and then apply the identical criteria employed in arriving at a conclusion with reference to indications for unilateral pneumothorax This rule applies whether or not one lung is already collapsed The condition of the collapsed lung must be carefully appraised If collapse is fairly complete, a decision must be reached as to whether it will be feasible to permit partial re-expansion before attempting collapse of the contralateral lung. It must be determined whether or not the disease in the contralateral lung is active and progressive, entailing a burden of toxemia which will not yield to the usual measures A just decision is often most difficult and can be obtained only after an exhaustive study, possibly carried over a period of weeks or months by one intimately acquainted with the problems arising in the diagnosis and treatment of pulmonary tuberculosis In many cases of bilateral tuberculosis, collapse of the more advanced lung will ultimately lead to improvement in the contralateral lung If this does not occur in a reasonable time, or if in the course of artificial pneumothorax for unilateral disease the contralateral lung becomes involved, or if reactivation of an old lesion in the contralateral lung should arise simultaneously, bilateral pneumothorax would be indicated.

Under application of bilateral gas therapy the general rules applying to technic vary but little. Moorman (*loc cit*) emphasizes that while the partial collapse is simultaneous, it is well to remember that the fillings should be given alternately, and if circumstances permit, collapse of one lung should be maintained 4 to 6 weeks, with an interval between fillings of 8 to 12 days, before collapse of the contralateral lung is attempted.

The occurrence of *hemorrhage* of magnitude is recognized as the 'most urgent indication for attempt at pneumothorax under any circumstances. Cohen (*loc. cit*) considers that in uncontrollable or persistent hemoptysis there is no treatment that can approach pneumothorax in promptness or effect. One injection of 500 or 600 c c of gas stops the bleeding as though the bleeding point had been ligated. Harms and Grunewald (*loc cit*) are of the opinion that the indication is urgent in severe hemoptysis.

*In tuberculous pleurisy with effusion* or *tuberculous empyema*, repeated aspiration with gas replacement is absolutely curative in 75 to 100 per cent of cases, according to the experience of Cohen (*loc. cit.*) The percentage applicability of pneumothorax therapy must depend very largely on the duration of the process before the patient comes under treatment at all, or before pneumothorax therapy is given consideration. R. W. Watson (Arch Surg 19:1175 (Dec—pt 2) 1929) records satisfactory results, so far as the actual technical application is concerned, in 40 per cent of those attempted; partially satisfactory results in 40, and that achievement of collapse was impossible in 12. Cohen gives the figures as 34 satisfactory; partial in 30, impossible 32.

*Complications* — The complications and unpleasant sequelæ have been made the subject of study in an effort to develop a technic which will reduce their occurrence. Chief of these unpleasant results in all probability is the tendency to *fluid formation*. J. D. Macfie and G. Napier (Brit J 1 442 (Mar 8) 1930) state that the probability of the occurrence of pleural effusion is quite outside of the physician's prognostic powers. Whether the fluid is due to tubercle, local anesthesia, cold air, too much gas, etc., it is quite impossible to say, though so far as untoward effects are concerned, these writers agree that the prognosis is not ultimately worse. Cohen (*loc cit*) is in accord with this view, stating, on the basis of a series of over 200 cases, that small *effusions* do not interfere with the course of the treatment and need no special attention. Large effusions can be avoided by not inducing compression too rapidly and by keeping the patient quiet in bed for the first 6 or 8 weeks. L. Boonschaft (Am Rev Tuberc 21:640 (Mar) 1930) advocated a rather prolonged treatment with **calcium chloride** intravenously as a prophylactic measure, giving 5 c c (1¼ drams) of a 5 per cent solution, thrice weekly for 4 to 5 weeks, then semiweekly for a similar period, and, finally, once weekly for an equal time. As justification, he reports development of effusion in but 1 of 15 cases under treatment.

The actual development of tuberculous *empyema* is a more serious complication and can be accounted for by the tearing of adhesions, and thus opening a superficial ulcerative process. A possible late spontaneous pneumothorax may account for empyema of other bacteriologic origin. Considerable optimism is shown by Cohen even under these

circumstances (he encountered this situation in 5 of 200 cases; Harms and Grunewald (*loc cit*) report 25 in their series of 800 cases—a quite similar ratio), and he remarks that tuberculous empyema cannot be considered a serious complication in the light of present knowledge. There was a time not so long ago when it was considered an incurable malady. In his series of over 200 cases he encountered this complication 5 times. Four of these were cured by the simple procedure of aspiration with gas replacement and injection into the pleural space of 2 c.c. of a 1:200 solution of neutral acriflavine at the end of each operation. Three to 6 operations clear up the pyoid fluid. The fifth case was cured by a Sauerbruch operation.

*Pleural shock*, the *bête noir* of the simple paracentesis, is rendered very unlikely by pleural anesthesia, slow injection and avoidance of high pressure. *Air embolism* incidence is reduced by pressure avoidance, and assurance that the needle is in a free sac large enough to develop manometric oscillations before injection is actually made. In present day practice the occurrence of either of the above is extremely rare.

Development of temporary *digestive troubles* is recognized as a direct result of the therapy in a small percentage of cases. L. Bonafe and H. Mollard (*Presse méd* 38:1277 (Sept 20) 1930) refer to these as “benign,” disappearing in a few weeks, and believe them to be due to mechanical effects on the stomach and liver. Macfie and Napier (*loc. cit.*) remark that the loss of weight in a large percentage is at the beginning noticeable, probably owing to altered metabolism caused by purely mechanical intervention and in some cases by displacement of the mediastinum.

The great barrier, from the standpoint of pathology, to the success of this form of surgical therapy is the presence of *adhesions*. Where no free pleural sac is found, pneumothorax treatment is necessarily abandoned. Where careful x-ray check indicates limitation of collapse by band-like or local adhesions, the application of the Jacobaens measures of **electric closed severance** is again demonstrated of great value by Watson (*loc cit*) and by W. Sachs (*Beitr z Klin d Tuberk* 74:204 (May 23) 1930). By the use of the later developed **electrocoagulation current**, in place of the electrocautery, heat and obscuring smoke are avoided.

The report of Sachs above noted and that of C. D. Parfitt (*Canad. M. A J* 22:170 (Feb) 1930) are sufficient warning against entertaining the idea of open operation for severance of adhesions where apparatus for the Jacobaens method is not available. These articles report the regular development of pleural effusions with open methods of severance, with the subsequent transition to empyema stage in approximately half the cases.

Desirable as the complete liberation of adhesions may be, their presence, when not extensive, does not always completely vitiate the value of collapse therapy, because even in their presence a partial rest, much greater than obtainable by medical means alone, can be maintained.

*Value, End-results*—A mathematical evaluation of the end-results of pneumothorax therapy is attempted by Cohen on the basis of comparison of the groups of recipients and nonrecipients. Of those in which he was able to compress the lung satisfactorily 100 per cent. are improving, and of those in which entire failure occurred, 16 per

cent are improving. In other words he found the chances for a moderately advanced case to improve to be just about 6 times as good with pneumothorax as without it. He cites Rist, of Laeunec Hospital of Paris, who concludes as a result of study of 800 cases of pneumothorax, as against a large number of cases in which artificial pneumothorax had been advised and was refused, that the end-results in those treated with pneumothorax were 7 times as good as among those who refused the treatment.

Fechter (*Ztschr f Kinderh* 49:143 (Feb 14) 1930) reports on 70 children of school age in whom pneumothorax was induced. Thirty were cured (42.8 per cent), 11 (15.7 per cent) became bacillus-free and showed improvement. Four did not improve, 12 became worse, and 13 died. In the patients with cavities, showing primarily advanced disease, the results were less favorable than in the rest with open tuberculosis, by the use of pneumothorax, however, 4 times as many patients with cavities were rendered bacillus-free as could have been rendered bacillus-free by purely conservative methods.

J. B. Amberson, Jr. (*Ann. Int. Med.* 4:343 (Oct) 1930) reviews 156 cases in which lung reexpansion had occurred an average of 5 years before the follow-up study. In 89 cases healing was good and the cavities were permanently closed. In 76 cases healing was incomplete and the cavities were not entirely closed on reexpansion. From his studies he came to the conclusion that in cavitation the total duration of treatment is not so important as the duration of the treatment after the cavity has become closed and the sputum negative. Maintenance of closure of from 1½ to 2 years proved desirable, making a total

treatment period in the successful cases of 2 to 3 years.

That the great value of this method is available outside sanatoria is well demonstrated by G. Poix and A. Bosnieres (*Presse méd.* 38:1513 (Nov 8) 1930) who used 47 home cases in a comparison with 124 hospital confined cases. They insist on the same careful pre-insufflation investigation of the local disease, and on the sufficiency of home surroundings for care between insufflations. The reinjections are made every week for a few months and then every 15 days. The patient remains in bed for 6 months, coming to the clinic for gas as often as above indicated and returning home practically immediately. They report an inability to observe any superiority in the results obtained by hospitalization.

**Thoracoplasty.**—Pneumothorax and phrenic exeresis are measures that may be employed relatively early in the course of tuberculosis. Though neither of these procedures is without danger, they have no prohibitive mortality. In the former, should complications arise, aspiration of gas can be done and pulmonary reexpansion secured; in the latter, a fixed effect has been produced but reduction in vital capacity has been reduced approximately but 30 per cent., and, as seen, this amount is chiefly at the expense of the pathologic lung area. Surgical measures, other than these, that are directed toward reduction of respiratory activity, involve a more or less extensive change in the thoracic walls themselves; and because of the permanence of the changes produced, and because of the operative hazard in securing them, serious consideration must be given toward determination of the indications for such operative work. After this question of indications has been

determined, equally serious consideration must be given to the questions of anesthesia, operative technic, division of the procedure into multiple stages, etc

*Contraindications.*—Enough reports have appeared to enable the surgeon, who has not had an immediate personal background of experience, to make a better selection of cases than did the pioneers in the early days of their work. Experience has shown that a relatively small number of patients fall into the group of those reasonably amenable to this form of surgical therapy, so that immediate recognition of contraindications is necessary

According to A. Maurer (J. de Chir. 36.857 (Dec.) 1930) thoracoplasty is contraindicated (1) when the lesions are bilateral, (2) when the lesions are progressive, the patients febrile and the pathology of the ulcerocaseous type; (3) when there are active lesions in other organs (except the larynx); (4) when there is sclerotic or emphysematous change in the other lung, (5) when the general condition of the patient is very poor. A. V. S. Lambert and F. B. Berry (Ann Surg. 91:57 (Jan.) 1930) regard any case in which there is distinct evidence of disease in the opposite side as having a poor prognosis, whether the lesion appears quiet or not, because of the difficulty in estimating the significance of the x-ray evidence of former disease. G. Hellsing (Acta med Scandinav. 71.521, 1929) emphasizes that thoracoplasty renders a lung permanently functionless, therefore the integrity of the other side must be assured. He believes also that patients over 45 should not, as a rule, be operated on.

E. Archibald (Canad. M. A. J. 21:502 (Nov.) 1929) speaks of a doubtful group where there is extensive infiltra-

tion in the diseased lung and cavities are multiple or large, where there are occasional periods of slight rise in temperature and pulse rate, where there has been loss of weight and strength with markedly positive sputum, and x-ray shows the other lung to be under suspicion, though also giving evidence of a reasonably good resistance in the form of scar-contraction on the evidently diseased side. He gives these cases surgical consideration because the prognosis without operation is poor. He lists as unfavorable cases those where the lesion is definitely progressive and cavitation extensive, with signs of more recent infiltration in the other lung.

*Indications.*—The actual indications for the consideration of this surgical step are well set forth by P. K. Brown (Ann Int Med 4.361 (Oct.) 1930), as follows: "It is the part of the tuberculosis specialist so to measure up a patient's chances from accurate determination of changes resulting from treatment, that he may say with reasonable degree of certainty, the time has come when the patient faces defeat, perhaps several years postponed, without the help of conditions which thoracoplasty alone may bring about.

"To illustrate this point that there is a right moment for thoracoplasty is the object of this presentation. To show it the more clearly, the cases presented are nearly all selected from a sanatorium run for young working women, where the visiting staff of 3 physicians, the director and a surgical consultant have seen and studied every case. The principles of care have been based on supplying to the full the recognized fundamental essentials of sanatorium care, with the introduction of only one variable at a time. A staff evaluation of progress in all doubtful cases is the rule,

and each successive step, whether it be postural rest, the use of tuberculin, the elimination of some disturbing physical handicap, the use of pneumothorax or some surgical procedure, has always been the result of conference . . . *It must be made clear that thoracoplasty is possible only when one side is well enough to carry the full load without danger of breaking down . . .* The rule that applies to pneumothorax applies also to thoracoplasty. The increased burden on the relatively good side must not be too great or applied when the lung is not in an arrested condition.

"Patients who have been for years struggling to close one-sided cavities without success are obviously good cases for thoracoplasty. They have good resistance but are dangerous to themselves and to others and must continue indefinitely to lead sheltered lives unless we can close the cavities. Where we find the shoulder low on the affected side, the diaphragm high and the heart, trachea and mediastinum pulled toward the diseased side, and still a cavity persists, thoracoplasty merely continues to its ultimate limit what nature has struggled, often for years, to accomplish without success."

These sound conclusions are supported by Hellson (*loc cit*), by P Bull (*Acta chir Scandinav* 66 553, 1931) and by P Schonwald (*Northwest Med* 29:177 (Apr) 1930) all after reviews of large series of cases.

**Anesthesia**—**Local anesthesia** is considered the method of choice by most operators, among them being O Schedtler (*Deutsche med Wchnschr.* 57 491 (Mar 20) 1931), who reported on a consecutive series of 320 cases from Ziegler's Clinic, Maurer (*loc cit.*); W. Sachs (*Beitr z klin. Tuberk* 74:254, 1930) and Schonwald (*loc cit.*)

A considerable group of operators, however, used **ethylene** or **nitrous oxide** in combination with the **local anesthesia**. I W Magill (1.295 (Feb. 8) 1930), Lambert and Berry (*loc cit*), and E W Archibald (*Surg Gynec Obst.* 50.146 (Jan—No 1A) 1931).

**Operative Technic**—Multiple stage procedure apparently is established as the method of lower mortality, concurrence in this opinion being found in the reports of Bull (*loc cit.*), Lambert and Berry (*loc cit*), 2 or more stages, Schedtler (*loc cit.*); more commonly 2 stages, Maurer (*loc cit*) Archibald (*loc cit*) says that we owe to Hedblom chiefly, in this country, and also to Keller, the principle of the *graded thoracoplasty*, which means multiple operations and but little at a time. The writer considers that there is no more certain way of playing safe, and at the present moment there is a distinct tendency, to which he heartily subscribes, toward a 3-stage operation.

There is some difference of opinion as to the value of the upper or lower attack at the onset of the operative series. Archibald (*loc cit*) states that after choosing the patient for operation, the chief danger arising lies in putting out of function suddenly too large an area of the diseased lung. It is the rule that the removal of from 4 to 6 inches of the lower fifth and sixth ribs increases the heart's rate by 20 or 30 beats for a period of a week or more. The extra labor is obviously considerable. If all the ribs are taken off at one sitting, as used to be advised by continental surgeons, even a healthy heart is frequently unable to stand the strain. A failing heart then brings on pulmonary edema. On the other hand, it is well known that if the mediastinum has been



stiffened by long standing fibrosis, or by a preexisting pneumothorax, or by chronic empyema, the extensive removal of ribs is much better borne by the heart, and the pulse rate, after operation, may rise but little. His warning, from the physiologic considerations, is not to take off too many ribs, nor too large a piece of each rib, at one time. As a possibly valuable point to consider in thoracoplasty is the suggestion of W. C. Meiss (Nederl tijdschr v geneesk 74 268 (Jan 18) 1930), who finds in dogs that rib degeneration is prevented if the periosteum is painted with 10 per cent formaldehyde solution.

*Results of Thoracoplasty*—Thoughtful surgeons and clinicians advise thoracoplasty only when a patient has made clear his resistance by fibrosis, but has obviously reached a stage at which sanatorium treatment can accomplish nothing further. With such material at hand, restoration of any considerable number to self-supporting activity is an economic advantage and a therapeutic triumph. Archibald (*loc cit*) in the group of "favorable cases" reports 66 per cent. of practical cures, i. e., patients restored to community life and able to work, with a further 13 per cent of great improvement. The operative mortality was but 4.3 per cent. In the second group, or of doubtful risks, there were 38 per cent of practical cures and 24 per cent of great improvements; while in the group carrying a bad prognosis, there were no practical cures and only about 20 per cent. marked improvements. The operative mortality in these 2 latter groups was 4.2 and 26 per cent respectively.

In 22 patients with no clinical or x-ray evidence of disease in the other lung, Schonwald (*loc cit*) reports 72 per cent as disease arrested. Schedtler

(*loc cit*) states that of the first 200 thoracoplasties at Ziegler's Clinic, 43.5 per cent are considered healed. Of 320 cases, consecutive, the fatal mortality within 8 weeks of operation was 5.3 per cent, but in uncomplicated unilateral cases 3.3 per cent. In a series of 64 unilateral cases observed by Lambert and Berry (*loc cit*), 36 per cent were cured and 25 per cent benefited, the operative mortality was 12 per cent.

Bull (*loc cit*) concludes that from 35 to 45 per cent of patients who cannot be saved by other means are rendered fully fit for work by thoracoplasty. About 20 per cent are benefited, but ultimately die of tuberculosis. About 20 per cent derive no benefit and about 10 per cent die as the result of operation.

Surgical procedures other than those dealt with in the preceding are but extensions or variations of these same measures directed toward securing collapse.

#### *Section of the Scalene Muscles.*—

This is receiving attention particularly in association with phrenic nerve operation and especially in upper lobe lesions where adhesions are extensive and prevent collapse of the cavity and coaptation of its walls. It is used either as an adjunct to phrenicotomy, where the collapse has not been complete, or in conjunction with the exeresis where preoperative study indicates the probability of incomplete upper lobe collapse. H. Els (Zentralbl f Chir 57 2228 (Sept 6) 1930) reports favorably on the procedure and in addition suggests its use in incomplete compression by pneumothorax therapy. J. W. Gale and W. S. Middleton (Arch Surg 23 38 (July) 1931), in addition, indicate its value as a preliminary to thoracoplasty, making more accessible the upper rib, by relieving the antagonism to the caudad pull

of the intercostals and also by therefore lessening the amount of rib resection necessary F. E. Koch (Beitr. z. Klin. d. Tuberk 73 751 (Oct. 23) 1930) gives a confirmatory report of the value of this procedure in 12 cases of unilateral involvement of the types noted

**Multiple Intercostal Resection.**—

This operation is suggested by J. Alexander (Am. Rev. Tuberc 20 637 (Nov.) 1929), where there is no very large cavity, but in which reduction of mobility and some collapse of the wall is desirable. He believes in certain instances it will prove a reliable substitute for the more formidable thoracoplasty

**Anterolateral Costectomy.**—According to C. A. Hedblom (Arch. Surg 21 1114 (Dec.—pt 2) 1930), this is but an extension of the principle of multi-stage thoracoplasty—applicable where the usual posterior thoracoplasty has not given sufficient lung collapse, though there may have been collapse of the average amount of the wall itself. Various factors may be responsible, *i.e.*, large cavities, rib regeneration in interval between stages, or incompletely obliterated empyema cavities. It involves removal of segments remaining after posterior thoracoplasty, the incision vertical in midaxilla, the axillary muscles raised by tunnelling beneath, and a greater lateral collapse is therefore obtained. In a series of 26 cases there was but one operative death. All recovered cases have bacillus-free sputum where any expectoration is still done; 16 patients are symptom-free except for dyspnea on exertion. Eight are greatly improved, showing varying grades of weakness, dyspnea on exertion and tachycardia.

**TUBERCULOSIS IN CHILDREN.—INCIDENCE.**—Further data as to the frequency of tuberculosis

in childhood are given by L. B. Dickey and R. P. Seitz (Am. Rev. Tuberc 23: 13 (Jan.) 1931). They did intracutaneous tuberculin tests on 3500 children of San Francisco. The incidence as recorded by their positive reactions was 5.6 per cent at 1 year of age, 20.6 per cent at 5 years; 26.2 per cent at 10 years, and 46.6 per cent at 14 years. It will be noted that these figures are considerably less than those given for the school children of Philadelphia as quoted in the SUPPLEMENT of 1931, Vol. X, page 918.

The opportunity for contact with open tuberculosis would seem to be the determining factor in accounting for the varying incidences of tuberculosis in different communities, provided, of course, that in comparative studies all tests are made after the same manner with equally measured doses of active tuberculin.

M. W. Barnard, J. B. Amberson, Jr. and M. F. Loew (Am. Rev. Tuberc 23 593 (May) 1931) found 67.3 per cent. positive tuberculin reactions in 1000 adolescent school children of New York City. The value of the tuberculin reaction in the detection of tuberculous infection and of the x-rays in revealing tuberculous lesions is illustrated in the following extract from their article.

X-rays were made of the chests of all of the children. Of these, 184 revealed evidences of tuberculosis, 71 were apparently healed, and 113 were interpreted as being clinically important.

Of the 184 positive x-rays, 11 would have been missed if the 327 cases with negative tuberculin had not been x-rayed. Only 25 of the 184 were graded "D" on general health; only 18 were 10 per cent. or more under weight; only 35 of the 1000 children gave histories of exposure to tuberculosis, and

of these only 8 had x-ray evidence of tuberculosis, and of 24 who had physical findings suggesting pulmonary tuberculosis, not one had an abnormal x-ray

H P Chadwick and D Zacks (*Ibid* 22 626 (Dec ) 1930) made a study of 42,071 children examined and given the von Pirquet tuberculin test over a period of 3 years The ratio of reactors in the 42,071 children studied in this series shows a gradual trend upward from 21 per cent infections at age 5, and 25 per cent at age 10, to 35 per cent at age 15 The average percentage for the entire group is 28 Different sections in the same city may show a wide variation in the percentage of reactors It was found in one city of 60,000 that the number of children reacting to the tuberculin test in different school districts varied from 11 per cent to 60 per cent The number of reactors increases with the opportunities that the child has for contact with bacillus carriers Persons with chronic forms of pulmonary tuberculosis, such as are found in granite quarry workers, expose and infect more children than persons with the more acute forms who live a much shorter time after the disease becomes infectious Crowded living conditions afford more opportunities for contact and congested areas show a higher percentage of infection Twice as many reactors are found among children with a history of direct contact with a case of pulmonary tuberculosis

Another factor to be taken into account is bovine infection In a few rural towns with a scattered population and less than the average number of pulmonary tuberculosis deaths, 38 per cent. of reactors were found The majority of the small towns, however, show a little less than the average percentage for the state as a whole The

boys of the Irish, Canadian, and Teutonic groups in this series show a much higher incidence of infection than the girls The death rate in Massachusetts for all forms of tuberculosis declined from 144 per 100,000 in 1917, to 73 in 1927 Three important factors have operated to bring about a reduction in the number of infected children (1) The steady death rate decline results in fewer persons with tuberculosis at large in the community to spread infection (2) The state has a little more than 1 bed per each tuberculosis death in which to segregate cases of tuberculosis and so further reduce the source of infection in the homes of these patients (3) Pasteurized milk is now available for about 60 per cent of the population of the state and by so much is the possibility of bovine infection curtailed.

R. P. Forbes, R Verploeg and M K Bazemore (*Am. J. Dis Child* 41 26 (Jan ) 1931) made a survey of tuberculosis in the school of a small community in Colorado, composed largely of health seekers, where contact with the disease is unusually great It showed 36.4 per cent of 283 children from 4 to 15 years of age to be infected. This is only a moderate increase over the incidence noted in nontuberculous communities X-ray studies of the 103 children giving positive reactions revealed childhood tuberculosis in 19, or 67 per cent of the whole group, the average for the country at large varying from 1 to 4 per cent. No child with the adult or exudative type of tuberculosis was found. Most of the children reacting positively and those having actual childhood tuberculosis were not born in Colorado, where this study was made Climatic factors in Colorado apparently exert a favorable influence in the protection of children against active

tuberculous infection. In this survey, the father was the source of infection in 64.8 per cent of the children giving positive reactions, and the mother in only 12.6 per cent. Symptoms of fatigue, undernutrition, and a history of frequent colds are said to be not reliable aids in the diagnosis of childhood tuberculosis.

These statistics are largely based upon findings with tuberculin tests. There is a widespread belief that the negative tuberculin reaction indicates that the individual is not infected with the tubercle bacillus. Such, however, is not the case. The negative tuberculin reaction indicates only that there is no allergic response to tuberculin in the particular tissue tested on the patient.

Frankl, Krause, Emerson, and Rosenberger observed that the tubercle bacilli found in the feces in cases of "closed" lymphatic tuberculosis were of biliary origin and this observation is confirmed by V. Mikulowski (*Am Rev. Tuberc* 21: 686 (May) 1930). The presence of these bacilli in the bile is a result of more or less intense bacillemia, which may be present in cases of lymphatic and osseous tuberculosis.

The results of a special investigation in Massachusetts into the health of school children between the ages of 5 and 15 years, which was begun in 1924, are reported by D. Zacks (*New England J Med* 204: 1037 (May 14) 1931). It is assumed, as a working hypothesis, that tuberculosis is contracted in childhood, and that those who survive the initial infection later develop the adult type of disease, as a result of a sufficiently massive reinfection. The age group of 5 to 15 years shows the lowest mortality figures, and it was hoped that investigation of that group might yield some clue to the mode of development

of the adult type of disease. More than half of the school children came under observation, 30 per cent were found to react to tuberculin skin tests. The reactors were subjected to an x-ray examination, physical examination being reserved for those showing definitely pathological x-ray appearances. Both childhood and adult types of tuberculosis were reported to the Board of Health, and immediate sanatorium treatment was recommended in all cases of pulmonary disease. In the year 1929-1930, 49,000 children were examined in the clinic, and 5000 in the yearly follow-up.

**ETIOLOGY.**—That the tubercle bacillus may be the end product of certain invisible elements contained in an ultravirus whose life cycle carries it through stages of very minute nonacid fast granules, then acid fast granules and finally to the acid fast bacillus, is the opinion of A. Calmette and J. Valtis (*Ztschr f Tuberk* 58: 402 (Nov) 1930). After injection of the ultravirus (derived either from the filtrate of a young culture of tubercle bacilli or from the filtrates from tuberculous organs), subcutaneously or intraperitoneally into guinea-pigs, they find an enlargement of the lymph nodes. Within 3 to 8 weeks they could demonstrate in stained specimens from these nodes all 3 of the forms mentioned above.

They are of the opinion that such early forms of tuberculous disease as pleural effusion and erythema nodosum may be caused by a so-called prebacillary granulemia and also that this may explain some of the transplacental infections of tuberculosis.

Experimental data is presented by K. T. Sasno and E. M. Medlar (*Tubercle* 12: 214 (Feb) 1931) that leave no doubt that it is possible to enhance

greatly the virulence of B C G if the culture is grown in a suitable environment. To determine the proper environment was not an easy matter, and to get the original culture to grow luxuriantly in the new environment was also difficult. It is essential to have the pH adjusted between 7.2 and 7.4. This has necessitated the titration of Sauton's medium just prior to the addition of the fresh rabbit serum and to the transfer of the culture, for the medium is rather unstable. Fresh unheated rabbit serum seemed to be essential for a rapid increase of virulence.

The factors that determine the virulence of pathogenic bacteria are but little understood, this being especially true for the tubercle bacillus. Environment plays an important part, but the factors necessary to produce the proper environment are largely unknown. From their study the authors believe that the pH of the medium is one important factor and that there are substances present in unheated normal serum which greatly assist the tubercle bacillus to regain its pathogenicity. B C G, when grown under such an environment, developed a virulence which was greater than that of any other culture of tubercle bacillus which the authors have had in their laboratory. For more than 6 months, since the return of virulence, they have kept this altered B C G culture on Petroff's egg medium. It is still virulent, but to a lesser degree.

Another fact of importance is that with the return of virulence the organism is equally pathogenic for guinea-pigs, calves, and rabbits. It would seem that the normal rabbit serum has made available substances which have made the culture equally virulent for various animals. The work substantiates

the observations of Petroff and Branch on the "dissociation" of B C G. They have not used the same method, but their end-results are similar. The gross appearance of virulent and of nonvirulent cultures is different. The virulent culture is smooth, veil-like, colorless, and easily emulsified. The culture of low virulence is rough, compact, often chromogenic, and emulsified with difficulty.

In their work, the authors have purposely taken the original culture without any attempt at "dissociation." There can be no question of contamination. It was possible to alter the original B C G culture in its gross appearance and in its virulence without resorting to isolation of single colonies. Since it is possible to bring about such a marked alteration of B C G *in vitro*, and since so little is known relative to the factors that enhance or retard the pathogenicity of the tubercle bacillus, it would seem essential to use great caution in any application of B. C. G. as a prophylactic vaccine against tuberculosis. Great care must be used in the selection of the culture medium for cultivation of B C G. if it is to be used as a prophylactic vaccine. The pathogenicity of B. C. G. varies greatly with the environment. While Calmette's observations point, so far, to the innocuousness of the vaccine, still all control over the tubercle bacillus and its actions is gone once it gains access to the tissues. B C G is not a "*virus fixé*" unless it is kept in a certain environment.

**Heredity.**—From personal observation of 1017 patients with tuberculosis, J. Stephani-Cherbuliez (Rev. méd. de la Suisse Rom. 50: 761 (Nov. 25) 1930) ascertained that 823 were descended from healthy parents, while only 194 were of tuberculous parentage. The

disease, as a rule, appeared earlier in the descendants of tuberculous parents. Among the descendants of healthy parents, the severe chronic forms or fatal forms of tuberculosis predominated, while among the descendants of tuberculous parents the benign forms were by far the most numerous. The author's results confirm those of previous investigations.

In discussing the subject of intra-uterine transmission of tuberculous virus by the mother of the child, E. Lévy-Solal, V. Oumansky and Jeannet (*Bull. Soc. d'obst. et de gynec.* 19 54 (Jan.) 1930) report a case in which the mother had active tuberculosis (cavities in both lungs, tubercle bacilli in large numbers in the sputum). The child was separated from her immediately after birth and died at the end of 2 hours. The mother died a few hours later. Autopsy on the child revealed entirely normal viscera, very slight tracheobronchial adenopathy, and slight enlargement of the mesenteric glands. A careful study of rubbings made of the tracheobronchial, mesenteric, and lumbar glands, failed to reveal any tubercle bacilli. Two rabbits inoculated with 10 c.c. each of the liquid obtained by crushing the glands removed at autopsy developed glandular lesions but no lesions in the viscera. A search for tubercle bacilli in an enlarged gland was unsuccessful. Nevertheless, a guinea-pig inoculated with the liquid obtained from this gland presented generalized visceral tuberculosis at the end of 6 weeks, and a fourth guinea-pig, inoculated with the liquid from crushed bronchial and lumbar glands of one of the 2 animals first inoculated, developed similar lesions in 7 weeks. Acid-fast bacilli were found in large numbers in the visceral lesions of the 2 animals of the second series.

As there were no placental lesions and as accidental infection can be ruled out because of the child's early death, intra-uterine transmission of the tuberculous virus from the mother to the child is the only explanation possible. The results of the successive animal inoculations are interesting as showing how the tuberculous virus, but slightly pathogenic in the child, increased in virulence by animal passage until it was able to produce typical tuberculous lesions and cause the death of a guinea-pig in 7 weeks.

Brindeau, in discussing this report, stated that studies made by himself and Cartier showed that in about two-thirds of the cases the tubercle bacilli passes the placental barrier.

Couvelaire cited a case in which tuberculous lesions in the guinea-pig were not obtained until the seventh passage.

F. Harbitz and S. Mordre (*Norsk. mag. f. laegevidensk.* 92:253 (Mar.) 1931) described a case of congenital tuberculosis of the lungs and spleen in a stillborn infant, born at term of a mother previously well. The possible relation of the tuberculosis to placental infection could not be established, as the placenta was destroyed before the tuberculosis was suspected.

**DIAGNOSIS.**—The definite diagnosis of tuberculosis in childhood continues to be a difficult problem. F. Eberson, J. P. Delprat and E. Wolff (*Am. J. Dis. Child.* 40:753 (Oct.) 1930) have made a critical study of a group of children who were suspected of having tuberculosis. They divided them into 2 groups. Those having a positive tuberculin reaction were placed in Group I and those with a negative tuberculin reaction in Group II. They were studied from the standpoint of certain symptoms, physical signs and x-ray observations which are commonly asso-



ciated with tuberculosis. The symptoms were: repeated diseases of the upper respiratory tract, cough, nervousness, lack of appetite, loss of weight or failure to gain, fatigue, night sweats, lassitude and elevation of temperature. The physical signs were d'Espine's sign, paravertebral dulness, malnutrition, dulness over the manubrium sterni, enlargement of the cervical lymph nodes, abnormalities of percussion and auscultation, phlyctenular processes, bone lesions and adenitis. The following x-ray observations were noted: hilus calcifications, increased lung markings, enlargement of bronchial lymph nodes, calcifications of bronchial lymph nodes, thickening of interlobar or apical pleura, peribronchial infiltration, primary focus and parenchymal tuberculosis.

In Group I, 36.9 per cent had no symptoms in contrast to a similar lack of symptoms in 42 per cent. of Group II. Of more interest, however, was the lack of difference in the percentages of occurrence of the various symptoms in the 2 groups. The differences were not greater than 7 per cent. except in the case of cough, which was 13.4 per cent more frequent in Group II. Of the various physical signs, paravertebral dulness showed the greatest variation in its occurrence in the 2 groups, being found 20.1 per cent more often in Group II. Next in order of greatest difference was malnutrition, being 10.4 per cent in favor of Group I. Hilus calcifications, increased markings, and thickened interlobar pleura occurred more often in Group I, whereas peribronchial infiltration was found more often in Group II. The remainder of the x-ray observations occurred about equally in the 2 groups.

In commenting upon these studies the authors say: "Observations that have

been considered in the past as pathognomonic of tuberculosis were associated with nontuberculous processes in the lung . . . Evidence that has been presented in this study showed that commonly accepted clinical symptoms and signs have no diagnostic significance unless they are definitely correlated with positive tuberculin tests and roentgen observations that are positive for tuberculosis."

On the other hand, children may have active pulmonary disease and present none of the usual symptoms or signs and may even appear to be well nourished and in a state of good health. E. L. Opie (J. A. M. A. 95:1151 (Oct. 18) 1930) calls attention to this and re-emphasizes the importance of intracutaneous tuberculin tests in the detection of tuberculous infection and repeated x-ray observations of the positive reactors in determining the presence of active disease. (See also Incidence. Barnard, Amberson and Loew.)

**Tuberculin.**—It is now generally agreed that the *Mantoux intradermal test* is more sensitive than the *Pirquet scarification* one, as well as lending itself to accurate measurement of dosage. Confirmatory data of this are cited by A. S. Pope (*Ibid.* 97:846 (Sept. 19) 1931). However, the difference between these 2 tests seems to be somewhat less in the detection of active tuberculous disease. Pope states that about 90 per cent of children with significant tuberculous lesions reacted to the Pirquet test.

Some writers would attempt to correlate the degree of infection or disease, as well as the prognosis, with the degree of the tuberculin reaction. S. L. Cummins (Brit. M. J. 1:336 (Feb. 23) 1929) says that tuberculin sensitivity is apt to be at its height in healthy but in-

fectured persons and to be greater in patients with benign infections than in those with far advanced tuberculosis. He does not feel, however, that prognostic importance can always be attached to these observations.

In contrast to this, Opie (*loc cit*) calls attention to the fact that all of their children with clinically manifest tuberculosis reacted to 0.01 mg. of tuberculin and in two-thirds of them the reaction was 3 plus.

J. W. Lobban (*Tubercle* 12:19 (Oct.) 1930) thinks that the comparative reactions may be of value in prognosis. He states that the earlier or the less extensive the lesions, the less tuberculin is needed to excite a reaction, and as the disease progresses the reaction will not only be less in extent but that a greater amount of tuberculin is apt to be required to induce a positive reaction.

The reviewer is inclined to agree with M. Pinner (*Am Rev Tuberc* 23:175 (Feb.) 1931), who states that the attempt to correlate allergy and immunity quantitatively is doomed to failure, because the 2 terms are incomparable concepts. Immunity cannot be measured in terms of allergy for the identical reason. The clinician should not try to correlate a strong tuberculin reaction with high immunity nor will he find the reverse relation to hold true.

Of importance to the practitioner is the evidence of J. D. Pilcher (*J A M A.* 96:1868 (May 30) 1931) that tuberculin dilutions of 1:10 or 1:100 may be kept for a year or more without practical loss of activity. These dilutions were kept at ice-box temperature. Sufficient evidence is not available regarding the keeping qualities at room temperature.

In order to make a comparison of the

*dermatubim test* with the von Pirquet, Moro, and Mantoux tuberculin reactions, B. Goldberg and B. Gasul (*Illinois M J.* 58:60 (July) 1930) examined 109 children. They report that 37 per cent were positive to the von Pirquet, 20 per cent were positive to the Moro, 39 per cent were positive to the Mantoux, and 39 per cent were positive to dermatubim. The dermatubim test is easy of application and offers no difficulty in interpretation. Owing to this fact, it is superior to the von Pirquet, in which interpretation is more difficult. Since dermatubim is applied without pain or discomfort, it is of more practical use than the Mantoux test, which requires technical skill in its application, is accompanied with some pain, and is not devoid of the possibilities of complications.

**Bacteria.**—The value of searching for tubercle bacilli in the contents from gastric lavage of infants who are suspected of having tuberculosis is attested by J. Ligner (*Ztschr f Kinderh* 50:505 (1930)), who reports the finding of tubercle bacilli in the lavaged stomach contents of an infant 7 months old. The tuberculin reaction was not yet positive. He suggested that infected persons may be sources of contagion in the preallergic state.

The use of artificial media for the culture of tubercle bacilli and their identification from suspected material is becoming more widespread, due to the efforts of such workers as Corper, Petroff and Sweany and Evanoff. A cultural method for the detection of tubercle bacilli in the blood stream has been described by E. Lowenstein (*Munchen med Wchnschr* 77:1662 (Sept. 26) 1930, 78:261 (Feb. 13) 1931; 78:1080 (June 26) 1931) which, if it proves to be practical, will mark a distinct advance in diagnostic equip-

ment He claims to have isolated the organisms from the blood stream in about 80 per cent of active cases of tuberculosis Of particular significance is his statement that he has found a bacillemia in early cases before there was evidence of tuberculosis by physical findings or x-ray observations

W Pfannenstiel (Deutsche med Wchnschr 55 2130 (Dec 20) 1929) claims to have decreased the time necessary for tubercle bacilli demonstration after guinea-pig inoculation The injection is made into the animal's popliteal lymph nodes If tubercle bacilli are present, lesions develop within the second week after inoculation The nodes may be removed and tubercle bacilli demonstrated in the stained material from the crushed node

**X-ray Diagnosis.**—In writing of chest x-rays of nontuberculous children suspected of having tuberculosis, E Wolff and R S. Stone (J A M A 94 458 (Feb 15) 1930) state that they found the average number of previous diseases per case varied only from 2.2 to 2.6 for the various groups, while the whole series varied between 1.4 and 1.8 per case The average age of the whole series was 8 years, the youngest patient being 2 years and the eldest 15 years It is of special interest that the group without increased markings in the upper lobes have a higher incidence of past respiratory diseases, especially bronchitis, measles, and pneumonia, than in the group with increased markings One group, with an incidence of previous diseases of 1.7 per child, with an average of 3.5 years, showed in comparison with the clinic group a higher percentage of multiple axial vessels at the hilum, a slightly higher percentage of multiple axial vessels up to 2 mm in diameter in the upper left part of the chest, in ves-

sels of 3 mm in either lung field, and a somewhat lower percentage of localized increase in the lung markings There was no increase in the number showing positive d'Espine's sign, vertebral dullness, paravertebral dullness, and dullness of the manubrium in the cases presenting multiple axial vessels at the hilum The definite impression gained by a survey of the entire study is that there are no marked variations in any of the groups X-rays of the chest in the children without acute illness and with negative tuberculin reactions may show single or multiple, large or small axial vessels in the hilum, multiple axial vessels up to 2 or 3 mm in diameter in the lung tissue, localized increased lung markings, localized pleural thickenings, or none of these shadows From this it is apparent that a diagnosis of tuberculosis of the mediastinal glands or of lung tissue cannot be based on the findings of the x-rays In this study no calcifications, glandular tumors or localized pulmonary infiltrations were found and no definite correlation was found to exist between positive x-ray findings and the clinical history.

**Tracheobronchial Glands.**—The fact that the caseated tracheobronchial glands in infancy and childhood are difficult to diagnose, is emphasized by P Armand-Delille and C Lestocquoy (Am J. Dis Child. 38 1125 (Dec) 1929) The difficulty is increased because the physical signs, such as dullness and d'Espine sign, are not constant, the Pirquet test also is not sufficient The only way to arrive at a proper diagnosis is to supervise all children who have been in frequent and close contact with a germ carrier, and to have good x-rays (frontal and lateral) carefully examined, comparing them with films from other cases in

which x-ray observations have been checked at necropsy

In connection with the demonstration of enlarged bronchial and mediastinal lymph nodes by *percussion*, E. Granstrom (Ztschr. f. Tuberk 55. 18 (Oct) 1929) calls attention to the fact that there is not a parallelism between the size of the bronchial lymph nodes on the x-ray film and the extent and intensity of the dulness in the interscapular space or over the vertebræ. He devised an interesting experiment. A rubber balloon filled with 70 c.c. of fluid and introduced into the esophagus as far as the bifurcation of the trachea did not produce dulness in the interscapular space or over the vertebræ. In the bodies of persons who had not died from tuberculosis and into which from 70 to 100 c.c. of agar solution was introduced in the region of the hilus, the percussion sound (methods of Kraemer and Koranyi) was not changed. In 5 bodies of children, aged from 1 to 3 years, a rubber balloon was introduced into the esophagus as far as the bifurcation of the trachea and filled with 50 c.c. of water, this did not produce a change in the percussion sound, so that it was impossible to determine by percussion whether the rubber balloon or the esophagus was empty or filled. Since the tracheobronchial lymph nodes attain such a size only in rare cases, the author believes that as yet anatomicopathologic proof of the clinical importance of tuberculosis of the bronchial lymph nodes in adults is lacking although the diagnosis of this condition is made relatively frequently.

Based on the x-ray examination of 109 children between the ages of 7 and 12 years, J. B. Hawes and E. Friedman (J. A. M. A. 92 609 (Feb 23) 1929) reached the following conclusions

1 No diagnosis of hilum tuberculosis should be made on x-ray evidence alone

2. The presence of enlarged tracheobronchial glands, as shown by the x-rays, in the absence of clinical symptoms, does not necessarily mean active hilum tuberculosis or indeed hilum tuberculosis of any kind

3 Calcification of the nodes, or any calcification as shown by the x-rays, particularly when previous films did not show any calcification, is an indication that a healing or healed process is being dealt with. In such cases, in the absence of clinical signs and symptoms, institutional treatment is not needed

4 Repeated x-ray examinations are of great value in studying the progress of each individual case. Absorption of the hilum shadow and increased calcification are indications that healing is progressing favorably

5 As far as the selection of children for preventorium and summer camps is concerned, definite and prolonged contact with an open case of pulmonary tuberculosis and a positive von Pirquet reaction should be the chief and practically the only requirements. Special attention should, of course, be given to underweight and poorly nourished children

**PROPHYLAXIS.**—The use of B. C. G. vaccination against tuberculosis is still in the experimental stage. The reports of its efficacy are conflicting. The majority of the favorable reports continue to come from the French. For example, B. Weill-Hallé and R. Turpin (Presse méd. 38 1699 (Dec 13) 1930) have vaccinated 944 children within the past 10 years; 395 of these have been more or less constantly exposed to tuberculosis since immunization, yet 95.1 per cent have remained in good health

Attention is directed by Berghaus (Deutsche med Wchnschr 56 1771 (Oct 17) 1930) to Calmette's statement that in the cities and districts of France in which nearly all the newborn are vaccinated against tuberculosis, the general mortality has decreased from 40 to 50 per cent and that the same observation has been made in Rumania, Greece, Belgium, Uruguay, and other countries. In order to determine whether this improvement was caused by the tuberculosis vaccination the author investigated the tuberculosis mortality of infants and children in Baden during the years from 1877 to 1929. A tabular report indicates that since 1924, the year in which Calmette began his method of vaccination, the tuberculosis mortality in Baden decreased from 8 to 3.5 for each 10,000 children in 1929, or about 55 per cent. This decrease, which is about the same as that observed by Calmette, was effected without tuberculosis vaccination. Of every 100 children who died in 1929, only 1.9 died of tuberculosis. This shows that the vaccination against tuberculosis is really not as important as some pediatricians seem to think, since 98.1 per cent of deaths among children are due to other causes.

Much more important than among children, is the combat on tuberculosis mortality among young people between 15 and 30 years of age. Of those who die between these ages, 35 per cent die of tuberculosis, and among these persons vaccination against tuberculosis is ineffective. Only by increasing the natural powers of resistance and by avoiding overwork and other factors detrimental to the health, can the tuberculosis mortality of young people be reduced. The author is convinced that the decreased tuberculosis mortality

among children is likewise mainly due to the better care now given to infants.

Further observations, which make it seem probable that the B C G organisms may become more virulent when their environment is altered *in vitro*, are recorded by K T Sasano and E M Medlar (Am Rev Tuberc 23 215 (Mar) 1931). They were able by cultural methods to increase the pathogenicity of B C G for rabbits, guinea-pigs and cattle. In view of these observations, which are in direct accord with those of Petroff, they think that great caution should be observed in the use of B C G for human vaccination. They call attention to "the fact that all control over the tubercle bacillus and its activities is relinquished once it gains access to the tissues."

From experiments with B C G anti-tuberculosis vaccination Prokopowicz-Wierzbowska (Rev franç de pédiat 6 191, 1930) found that the B. C. G. vaccine had no ill effects on newly-born children, also that exogenic agents, such as bad hygienic conditions, defective diet, contagious diseases, and digestive or respiratory disorders, exerted no influence capable of increasing the virulence of the B C G stock and did not determine the appearance of tuberculosis in the child. Children thus vaccinated who lived in healthy surroundings did not develop tuberculosis. The vaccinations determined an allergy that was shown by the von Pirquet reaction in children living in an atmosphere free from the taint of tuberculosis. Some of the vaccinated children who lived exposed to a contagious form of tuberculosis were infected (positive von Pirquet reaction) but did not contract the disease. In rare and exceptional cases in which the children were not isolated after vaccination, early infec-

on did result in severe forms of the disease. The author states, finally, that it is indispensable to isolate the children who are vaccinated, during the time specified by Calmette.

Rohmer and Chaussinand (Bull et mém Soc méd d hôp de Paris 53:365 (Dec 2) 1930) direct attention to the importance of removing infants from a tuberculous environment for from 6 to 8 weeks after vaccination by ingestion of **B. C. G.**, as long as immunity is not established. Of 4 infants who had been vaccinated, 3 died; in the fourth a nonvirulent type of tuberculosis developed. In all instances the parents were tuberculous.

Since 1924, over 210,000 children have been vaccinated against tuberculosis by the **B. C. G. method.** A Calmette (J A M A 94:1723 (Mar 1) 1930) secured this information from physicians and health officials who use vaccine in various countries. More than 20,000 clinical researches have proved the harmlessness of **B. C. G.** vaccine in man and beast and its efficacy has been proved by the fact that infant mortality has been reduced one-half in France, where vaccination in the newborn is systematically carried out.

In Thann, Alsace, says the report, the vaccinations have increased rapidly since 1926, 76 per cent of the newborn were vaccinated in 1928. As a result, the mortality has dropped from 66 per cent to 2 per cent. Furthermore, the children develop better, and are more resistant to infections. The Institut Pasteur de Paris has created a special laboratory for the preparation of the **B. C. G.** vaccines, at present supplying 300 tubes of vaccine a day. The vaccine is furnished gratuitously to physicians and midwives who request it.

From 1927 to May, 1930, P. Drucker

(Ugeskr f læger 93:558 (May 21) 1931) vaccinated orally, according to Calmette, 49 infants exposed to tuberculosis at home, 19 of these being exposed to open tuberculosis. During the first year of life 4 died from nontuberculous disorders. Neither history nor objective after-examination in the remaining 45 afforded any evidence that these children, apart from the positive tuberculin reaction, are infected with human tuberculosis, and continuation of vaccination with **B. C. G. vaccine** seems justifiable. He favors intracutaneous, rather than oral vaccination. With both Pirquet's and Mantoux's tests in 40 of these cases, allergy was established in 95 per cent, and by Pirquet's test alone, only in 52 per cent.

The results of an extensive investigation of the effects of vaccination of nursing with **B. C. G.** were reported at the Seventh Conference of the International Union Against Tuberculosis, held in Oslo in August, 1930. A Calmette (Ann de l'Inst Pasteur 45:525 (Nov) 1930) says that the absolute innocuousness of the vaccine was again confirmed by bacteriologists from many nations. No basis was found for the recent claims that certain strains of **B. C. G.**, *vis*, type S (smooth), could be isolated, which would produce progressive tuberculous lesions; the investigators were unable to isolate such strains themselves, and their examination of cultures furnished them of type R (rough) and type S, showed that both had been contaminated by other virulent bacteria.

Reports from all the countries of Europe except Austria, Great Britain and Portugal, and from Argentina, Brazil, Canada, Chile, the Belgian Congo, Cuba, United States, Japan, Maurice Island and Uruguay, showed



that systematic vaccination of nurslings with B C G had produced a marked decrease in the general mortality from all causes among nurslings. It was noted, moreover, that the mortality during the first month of life, before the effects of the vaccination have time to be manifested, remains approximately the same among vaccinated and nonvaccinated infants. This seems an additional reason for attributing the decreased number of deaths during the first year to the effects of vaccination with B C G. The general mortality was diminished by about 50 per cent by the vaccination, while deaths from tuberculous infection were practically eliminated. Since the deaths from tuberculosis have never been more than a very small proportion of the total number, it is logical to assume that vaccination with B C G increases the infant's resistance not only to tuberculosis but to other infections as well.

G Pittaluga and F Garcia (Arch cardiol y hemat 10 353 (Oct) 1929) made a *hematologic* study of the *variations* of the leukocytic formula in 120 newborn infants, aged from 3 to 12 days, in 110 just before and during the period of B C G vaccination, and in 10, who did not receive vaccination, as a control. Blood for analysis was taken in all cases at the same time and under similar conditions. In the groups of vaccinated infants, from 3 to 8 analyses were made, the last 4 or 5 being made at 15-day intervals. The entire period of observation lasted for about 3 months. In the control group only 2 analyses were made, at an interval of from 3 to 6 days, during the first fortnight of life. A dose of B C G vaccine diluted in a teaspoonful of mother's milk was given to the infant every other day for 6 days.

In 22 per cent of their patients the authors observed a spontaneous monocytosis, which was present before the administration of B C G vaccine and was independent of it. It rose to 20 or more monocytes per 100 leukocytes between the fifth and twelfth days of life. In this group, after vaccination, the monocytosis temporarily diminished and then increased again. The authors consider this change an inversion of the normal monocytic reaction after vaccination. In all the other cases an early monocytosis appeared after vaccination. The monocytic reaction was unquestionable in the author's case.

A monocytosis of 15.5 per cent was observed between the 2 first weeks after vaccination, whereas in the blood of the infants before vaccination, as well as in the blood of infants in the control group, the monocytes remained between 6 and 9 per cent. These variations correspond to those which have been reported so frequently in the American literature, in which the importance of the monocytic reaction in tuberculosis has been repeatedly emphasized.

Pittaluga and Garcia conclude that the oral administration of B C G vaccine caused in their cases a general reaction characterized by early and marked monocytosis followed by lymphocytosis of long duration, diminution of the neutrophil granulocytes and deviation to the left of the number of nuclear lobes (Arneth). These leukocytic alterations represent a cellular reaction of defense of the patient after vaccination, against the vaccine virus. This reaction is of the same type as the local and hematic reaction characteristic of primary tuberculosis, though in the case of vaccination it has a more rapid evolution, as it is observed in the cycle of leukocytic modifications of the blood.

The opinion is expressed by R Chaussinand (Ann de l'Inst Pasteur 45 71 (July) 1930) that the sole advantage of the intramuscular route for injection of B C G vaccine over other methods is the rapid appearance of allergy. Doses of 0.05, or even sometimes of 0.02 mgm, generally produce a positive cuti-reaction at the end of 3 or 4 weeks, whereas this reaction appears only toward the sixth week after a subcutaneous injection. Two simultaneous intramuscular injections of 0.025 mgm each would have a beneficial effect on newborn children who cannot be isolated from their infectious surroundings and in whom it is desirable to produce a rapid immunization.

In some cases the *subcutaneous vaccination* of children with B C G is without noticeable change, according to A. Brinchmann (Norsk mag f Laegevidensk 91:1119 (Oct) 1930), while in others an infiltration or abscess appears at the place of injection and may require up to a year's time for healing. In some cases the general state of health is affected, perhaps for half a year, but the traces disappear before the end of the year. Revaccination of children with B C G during the first 3 or 4 months accelerates both the appearance of the infiltration and the positive tuberculin reaction; signs of Koch's phenomenon may be noted. Examination of the blood of the vaccinated child shows little deviation from the normal, but in individual cases there may be a slight anemia and shifting to the right of the leukocyte formula.

The results of subcutaneous vaccination with B C G in 443 young persons have been reported by J. Parisot and H. Saleur (Presse méd. 38 129-144 (Jan 29) 1930). Among this number there were 46 persons 12 or more years of

age, 16 infants less than 1 year old, with the exception of newborn infants, and 57 between the ages of 1 and 2 years, the others were between the ages of 3 and 11 years. One hundred and forty-four persons had been vaccinated more than 2 years previously and 289 more than 1 year before.

The results of cuti-reaction tests on 169 persons who had been immunized from 3 weeks to 27 months previously showed that the cutaneous allergy appeared most frequently between 1 month and 6 weeks after inoculation. It was found to be positive in 105 persons, or in 62 per cent. This corresponds with the author's previous observations on the results of immunization of infants by the ingestion of B C G. With the exception of newborn infants, the morbidity and mortality of tuberculosis in vaccinated persons of all ages and living in both healthful and tuberculous environments was found to remain 0.

Regarding the occurrence of *fatal tuberculosis* following *vaccination* with B C G, E. Jaso (Arch de méd d enf 34 169 (Mar) 1931) reports the case of an infant admitted to the hospital at the age of 13 months, undernourished, undersized, rachitic, and with pyodermitis. Mendel's test gave a negative reaction at 3 different times, 40, 75, and 90 days after her arrival. Immediately after the third negative tuberculin reaction, she was vaccinated subcutaneously with 0.0125 mgm of B. C. G. There were no immediate abnormal reactions either local or general. Four months later the child presented a syndrome of progressive cachexia with superior left lobar infiltration and cavitary indications. Before a therapeutic pneumothorax could be established, the condition became generalized, evolving rapidly toward death. It is altogether

improbable that the generalization and fatal evolution were the result of the B C G vaccination, especially in the face of the absence of both immediate local reactions and enlargement of the regional lymph nodes. Nor is it reasonable to suppose that a child who had lived for 3 months in the same environment would yield more readily to a chance infection after vaccination than before. The author feels, therefore, that the infection must have been present before the vaccination, in spite of the negative tuberculin reactions, and that the benignity of the condition (only an extremely mild infection is not revealed by Mendel's test) was changed to a generalized and fatal form of tuberculosis by the B C G vaccination. To avoid such unfortunate accidents, it is advisable to take all possible precautions to detect a possible infection before vaccination with B C G.

**TREATMENT—Diet.**—The Gerson-Sauerbruch-Herrmansdorfer diet has received considerable comment in the past 2 years, little of which is convincing as to its efficacy in the treatment of tuberculosis. A Wolff-Eisner (Beitr z Klin d Tuberk 73 829 (Apr 23) 1930) points out that there are so many factors (low sodium chloride, high minerals, low carbohydrate, overfeeding, high vitamins, and phosphorus in cod-liver oil) involved that its evolution from a theoretical standpoint is not possible. Practically he has not been impressed by the results obtained from its use. H. Schmiedeberg (Monatschr. f Kinderh. 48:230 (Oct) 1930) reports that a good proportion of his younger patients lose their appetite when placed on this diet.

A salt-free diet was employed by G. Apitz (Deutsche med Wchnschr. 55:1918 (Nov 15) 1929) in the treatment

of 53 children with various forms of tuberculosis. In the beginning, all patients showed an increase in weight. Tuberculosis of the skin was influenced favorably, but the diet had no effect on the pulmonary processes. The author states that for the therapy of tuberculosis of the lungs, dietary treatment should be abandoned, because it is without effect. It is also pointed out that the sensational publicity which was given this treatment has been harmful, as many patients with progressive pulmonary tuberculosis are overconfident in its effectiveness and refuse any other treatment.

**Calcium.**—B. Varela, P. Recarte and J. Esculies (Ztschr f Tuberk 57 380 (Sept) 1930) have studied the blood of patients with pulmonary tuberculosis. The hydrogen-ion concentration, the carbon dioxide content, the total calcium of the serum and the fraction of ionized calcium were always within normal limits. During treatment the acid-base balance of the blood remained constant and the total and ionized calcium remained within normal limits.

Whereas a good many workers question the benefit to be derived from calcium therapy, H. G. Sholtz (Beitr z. Klin d Tuberk 78 243 (Aug 20) 1931) reports such benefits in patients with early tuberculosis lesions as marked reduction in expectoration in 80 per cent, lowering of temperature in some, and a subjective feeling of improvement in many. X-rays did not show any improvement of the lesions. He gave 10 c c (2½ drams) of 10 per cent. solution of calcium gluconate every other day.

**Ultraviolet Irradiation and Vitamin D.**—Closely associated with the supposed benefits to be derived from calcium administration is the effect upon calcium-phosphorus metabolism of ultra-

violet irradiation and vitamine D administration. From a clinical standpoint there is considerable belief that healing is more rapid in certain tuberculous processes, such as tuberculosis of the intestines, of the lymph glands and of the bones, after ultraviolet irradiation and perhaps to a somewhat less extent after administration of vitamine D preparations with or without calcium.

The experimental data is still rather confusing. B. Kramer, H. G. Grayzel and M. J. Shear (Proc Soc Exper Biol and Med 27:144 (Nov) 1929) quoted in an editorial (J A M A 94:413 (Feb. 8) 1930) observed 2 groups of tuberculous children. Each group was on an adequate diet and one group received large doses of viosterol. No differences could be detected between the 2 groups at the end of 12 months.

Other data of these same authors suggest that patients with intestinal tuberculosis did equally as well on cod-liver oil, cod-liver oil concentrate and irradiated yeast together with orange juice as with ultraviolet irradiation. Equal improvement was not noted with irradiated cholesterol. Based on these facts the editorial significantly concludes: "These observations suggest that such therapeutic value as cod-liver oil possesses in tuberculosis does not depend

on its relatively high concentration of vitamine D."

### *Artificial Collapse of Lung.\**—

Artificial collapse of the lung in selected cases of pulmonary tuberculosis in children is being more and more used. In addition to the more common means such as pneumothorax and phrenicotomy, the use of oil or so-called oleothorax is being employed. P. F. Armand-Delille and J. Giroux (Bull Soc de pédiat de Paris, 28:170 (Apr) 1930) have had success with such treatment in children. According to these writers, its use is indicated in those cases in which adequate collapse of the lung is not maintained by pneumothorax and particularly so in those cases where there are adhesions or where adhesions tend to form. They report 1 case with a clinical cure after treatment with a bilateral oleothorax.

L. Boonshaft (Am Rev Tuberc 21:640 (May) 1930) reports the lessened occurrence of pleural effusions in artificial pneumothorax when these cases are treated with calcium chloride intravenously. He gives 5 cc (1¼ drams) of a 5 per cent solution intravenously 3 times a week for 4 or 5 weeks.

## **TUBERCULOSIS OF THE LARYNX.** See LARYNX

## U

**ULCER, PEPTIC.**—Chronic ulcerations of the stomach and duodenum have long been among the most bitterly debated of controversial subjects. From the voluminous literature it will be possible to select only a few of the more recent contributions for the present discussion.

### **ETIOLOGY.—Vascular Lesions.**

—The relationship of vascular lesions to peptic ulcer has been studied by C. B. Schutz (J A M A. 96:2182 (June 27) 1931). A review of previous literature revealed that Virchow, in 1853, ex-

\* See also Tuberculosis, Pulmonary Surgical Treatment

pressed the belief that peptic ulcer may result from faulty blood supply. By vessel injection, Reeves demonstrated poorer vascularity in the ulcer areas of the stomach and duodenum. Payr produced gastric ulcers by inducing endarteritis, and as far back as 1883, F. Rosenbach produced ulcers by prolonged vasoconstriction. Sterile emboli were shown to produce peptic ulcers, in the work of I. Honda (Virchow's Arch f path Anat 266 549, 1927).

Schutz reported his study of serial sections of 30 specimens of peptic ulcer obtained at autopsy. All specimens showed arterial obstructive lesions in the vicinity of the ulcer. In 70 per cent definite embolism was found, while the remaining 30 per cent showed evidence of other arterial disease (endarteritis, arteriosclerosis, etc.). The ulcers were associated in 66 per cent, either with disease capable of producing embolism (endocarditis, etc.), with generalized arterial disease, or with infarcts in other organs. Schutz was able to find in each case vascular lesions in the vicinity of the ulcer which he could identify as antedating the ulcer, as distinguished from the secondary vascular changes always found surrounding the periphery. These secondary changes, he believes, are responsible for the extension and chronicity of the lesion, while the primary vascular lesion is responsible for the development of the ulcer originally.

**Hyperchlorhydria.**—The exceedingly frequent occurrence of hyperchlorhydria in ulcer has led many to attribute the ulcer to this factor. L. R. Dragstedt and A. M. Vaughn (Arch Surg 8:791 (May) 1924) demonstrated that gastric juice would not digest living mucous membrane of the stomach, duodenum, jejunum or colon.

Other workers have shown, however, that high acid secretion delays healing of acute ulcers. Ivy and his associates have produced experimental ulcers in animals by interfering with the normal neutralizing effect of biliary and pancreatic secretion. Clinically, it is well known that some degree of neutralization of gastric acid results in symptomatic relief and an apparent increase in healing. W. L. Palmer (Arch Int Med 46 165 (Aug) 1930, R. C. Brown J A M A 95.1144 (Oct 18) 1930).

S. J. Fogelson (J A M A. 96.673 (Feb 28) 1931) has introduced gastric mucin as an effective neutralizer of gastric acid. M. S. Kim and A. C. Ivy (J A M A 97 1511 (Nov 21) 1931), working with dogs with a biliary fistula, were able to show that mucin prevented the development of duodenal ulcer. The control animals, subjected to the same operative procedure but not treated with mucin, developed ulcers in 60 per cent of cases.

It must be admitted, therefore, that hydrochloric acid has some etiologic importance in the development of experimental peptic ulcer.

**Bacterial Infection.**—In clinical experience, the importance of focal infection in peptic ulcer cannot be denied. Rosenau and his associates have applied the principles of selective localization to this problem. A. C. Nickel (Ann Int Med 3 1084 (May) 1930) was able to produce stomach lesions in rabbits from organisms obtained both from foci and from the base of the ulcer. In duodenal ulcer, experimental gastric lesions were produced in about 50 per cent of rabbits receiving injections prepared from foci in teeth, tonsils and prostate, and in 72 per cent of those receiving organisms from the original

ulcer In gastric ulcer, 64 per cent of the rabbits developed gastric lesions from bacteria obtained from all the above sources

Control cultures obtained from 94 patients without gastrointestinal disease only produced gastric lesions in 9 per cent of rabbits injected

**Diet.**—That irritating food substances may be important etiologically in peptic ulcer has been suggested by S. Bergsma (Arch. Int. Med 47:145 (Jan) 1931) in a report concerning peptic ulcer in the black race in Abyssinia. In 2 years he had seen over 200 cases of peptic ulcer in the negro, many with pyloric obstruction. Sixteen patients who permitted operation showed multiple ulcers or scars. During the same period of observation no peptic ulcers were seen among the 5000 white inhabitants. Reports from Bellevue Hospital, in New York, were cited in which only 2 of 164 cases of peptic ulcer were negroes (M. Sturtevant and L. L. Shapiro: Arch. Int. Med 38.41 (July) 1926). Although intestinal parasitism and syphilis are very common in Abyssinia (both estimated at 90 to 95 per cent), this factor alone is hardly sufficient to account for the higher incidence of ulcer among the Abyssinians as compared with the American negro. Bergsma believes that the cause lies in the character of the native diet, consisting of sour black bread and pepper sauce (which contains about 50 per cent cayenne pepper). This diet is followed regularly from the age of 2 until death.

In ulcer therapy there is little doubt of the value of bland diets. Experimentally, G. B. Fauley and A. C. Ivy (Arch. Int. Med 46 524 (Sept) 1930) surgically produced simple gastric ulcers in rabbits and found that a rough diet definitely delayed healing, providing

some other irritating condition (silk suture) acted simultaneously

**Constitutional and Neurogenic Factors.**—The work of G. Draper, H. L. Dunn and D. Seegal (Am. J. M. Sc 169 322 (Mar) 1925) emphasized the relation of certain constitutional characteristics to visceral disease. They described the "ulcer habitus." Other writers have referred to the "ulcer type." This type of individual is apt to be high-strung, emotional, intense, and worrisome. Recent work reported by G. W. Crile (J. A. M. A 97 1616 (Nov. 28) 1931) associates peptic ulcer with other diseases caused by vegetative nervous system imbalance. Certain diseases, including hyperthyroidism, neurocirculatory asthenia, and peptic ulcer are the products of civilization with its increased nervous strain, according to this writer. Inasmuch as the suprarenal glands are the keystones of the vegetative system, he has practiced **suprarenal denervation** in resistant cases with definite improvement. Although the number of ulcer patients so treated is small, he feels that the method shows considerable promise.

Moses Einhorn (Am. J. M. Sc 179 259 (Feb) 1930) analyzed 1000 *recurrences* of gastroduodenal ulcers and found that in 7 per cent the recurrence could be directly traced to increased "psychic load." Many authorities believe that the incidence is higher than this.

As the knowledge of endocrinology and the vegetative nervous system increases, it is becoming more apparent that a close relationship exists between functional disorders and peptic ulcer.

#### **SYMPTOMS AND DIAGNOSIS.**

—The high incidence of peptic ulcer in patients with gastrointestinal symptoms has been emphasized by Alvarez, who



found duodenal ulcer in second place and gastric ulcer in fifth in a series of 175 cases of organic gastrointestinal disease. The 2 comprised 27 per cent of the series. The most frequent finding was gall-bladder disease.

Although a detailed description of the symptoms and diagnosis of peptic ulcer is impossible here, certain findings have received attention in recent literature. An analysis of the symptoms in 1224 cases of peptic ulcer, reviewed by Brown (*loc cit*), revealed that the average age at onset was 35 years, with  $7\frac{1}{2}$  years being the average time elapsing between the onset of symptoms and observation by the author. Forty-nine per cent described their subjective complaint as distress, while 51 per cent had actual pain. Typical food relationship was present in 1143 of the 1224 cases, the greatest number having pain from 2 to 3 hours after meals. Night pain occurred in no less than 34 per cent. Massive hemorrhage prior to admission was reported in 19 per cent, while an additional 6 per cent reported hemorrhage following medical treatment, giving a total of 25 per cent of patients having gross hemorrhage at some time. Perforation occurred in 4 per cent.

Gastric analysis by the Ewald technic showed that less than 3 per cent had a free acid below 20, 22 per cent had acid values between 20 and 40; and 75 per cent had free acid values above 40.

An analysis of a series of 199 cases of hematemesis operated on at The Mayo Clinic revealed that 78.3 per cent had peptic ulcer, and 12.1 per cent carcinoma of the stomach (Proc Staff Meetings Mayo Clin (Feb 11) 1931).

H. L. Bockus, C. Glassmire and J. Bank (Am J Surg. 12:6 (Apr) 1931) have emphasized the importance of *fractional gastric analysis* in the diag-

nosis and treatment of duodenal ulcer. Two hundred cases were studied, using the bread and water meal, followed by 8 extractions at 15-minute intervals. An analysis of the fasting contents revealed that 19.5 per cent had subnormal acidity, 20 per cent were classed as normal, while 60 per cent had hyperacidity, of which 13 per cent showed a free acid above 60 and total acid above 70. Eighty-four per cent showed definite postmeal hyperacidity, while subnormal values were found in only 8 per cent. The vast majority of these patients had ascending acid curves after the test meal with the highest figures being reached at the 2 hour extraction. Gastric motility was estimated by an examination of the fasting overnight residuum and the 2 hour extraction. Rapid emptying occurred in only 2.5 per cent, while 54 per cent showed various grades of motor delay. The authors believe this method of determining motility is of more diagnostic value than the information obtained by a 6-hour x-ray study.

The finding of pathologic products in the gastric secretion is believed by the authors to be of considerable diagnostic importance. Bile was present in the fasting residuum in 51 cases and 36 additional patients had bile in more than 4 of the postmeal fractions. Occult blood was found in the gastric extractions in 14 per cent. of cases, its presence in only those fractions showing bile being very suggestive of a bleeding duodenal lesion.

Repeated analyses during the course of treatment showed that while the initial degree of hyperacidity had no definite relationship to the development of recurrences, persistent or increasing hyperacidity during treatment favored return of symptoms. Persistence of more than a moderate degree of motor delay,

as judged by this test, is an indication for surgery in the opinion of these writers

The importance of a thorough diagnostic survey in peptic ulcer has been stressed by H R Hartman and A B Rivers (Arch Int Med 44 315 (Sept) 1929) They studied 1075 operated cases of peptic ulcer and found that 57.7 per cent had associated pathology in the abdomen Of the total, 41.6 per cent had evidence of a diseased appendix, 4.2 per cent had both gastric and duodenal ulcers, and 3.1 per cent had cholecystitis This latter finding occurred in 2.1 per cent of the gastric ulcer and in 3.6 per cent of the duodenal ulcer cases

**PROGNOSIS** — W C Alvarez (Am J M Sc 178 777 (Dec) 1929) quoted Einhorn and Crohn on the results of treatment of 100 cases of peptic ulcer as follows 86 were cured, but within 1 year 31 per cent had recurrences The percentage of recurrences increased to 50 per cent in 4 years By this time 19 had been operated on, leaving 27.3 per cent apparent cures after careful treatment

Severe hemorrhage occurs at some time in from 15 to 30 per cent, about 1 per cent having fatal hemorrhages, according to this author Balfour is quoted as finding a history of gross bleeding in 18 per cent of 1072 operated duodenal ulcer cases According to Alvarez's figures, hemorrhage is 6 times more frequent in men than in women Perforation occurs 7 times more frequently in gastric than in duodenal ulcer

This writer further states that 1 out of every 7 cases of apparent gastric ulcer at The Mayo Clinic in 1926 proved to be malignant. Almost every gastric ulcer larger than a half dollar was carcinomatous.

R C Brown (*loc cit*) has reported the results of treatment in 1224 cases of peptic ulcer Two general conclusions are drawn from the clinical study of these cases (1) that by far the greater proportion of peptic ulcers can be healed by proper medical measures; and (2) that these lesions tend to recur and do recur in a large percentage of patients, either at the original site or in a different area of the stomach or duodenum It is suggested that it may soon be realized that a peptic ulcer is a manifestation of a deep seated disorder

Of the 1224 cases reported, 1130 were treated wholly medically, while 94 were referred for surgery Check up by questionnaires and interviews of the medically treated cases showed that 66 per cent had good medical results (49.5 per cent cured, 16.7 per cent greatly improved) Ten per cent reported fair medical results (improvement) Of the 223 patients (20 per cent) who reported poor medical results, 31 were not improved, 155 were subsequently operated upon, and 37 had died from ulcer or its effects

The importance of differentiating pyloric obstruction due to pylorospasm from that due to cicatricial stenosis is emphasized. The author believes that the chief source of failure of medical treatment is organic obstruction These cases obtain most complete and permanent relief from surgery followed by a brief medical plan

**TREATMENT.**—Most internists and conservative surgeons are agreed that medical treatment should be given a thorough trial in the absence of definite surgical complications Failure of adequate medical therapy to result in cure, the development of perforation, pyloric obstruction, repeated massive hemorrhages, or a reasonable suspicion

of malignancy, indicate **surgical intervention**, in the opinion of S M Jordan (New England J Med 203 917 (Nov 6) 1930)

**Alkalis**—The value of alkaline therapy has been studied experimentally by W L Palmer (Arch Int Med 46 165 (Aug) 1930) Fifty-four ulcer patients were divided equally into 2 groups Both groups were fed 3 ounces (90 cc) of milk and cream every hour from 7 A M to 7 P M with 5 additional feedings of cereal or custard One group received alkalis hourly from 7 30 A M to 7 30 P M, with extra doses at 8 and 8 30 P M, given in 3 ounces (90 cc) of water The average daily dose of alkali was **sodium bicarbonate** 26.3 Gm ( $6\frac{1}{2}$  drams); **calcium carbonate** 20.7 Gm ( $5\frac{1}{6}$  drams), and **magnesium oxide** 3.3 Gm (50 grains) The second group received 3 ounces (90 cc) of **beef tea** instead of the alkalis at identical intervals

The degree of healing was estimated by the response to the "acid test," which consisted of the instillation of 200 cc ( $6\frac{2}{3}$  ounces) of 0.5 per cent hydrochloric acid into the stomach It was found that spontaneous pain disappeared in an average of 26 days in the alkali group, while it persisted for an average of 26.6 days in those receiving beef tea The "acid test" was negative under alkalis after 9.7 days (average), while it remained positive for an average of 26.9 days in the tea group Titrations of stomach contents obtained each night showed about twice as much secretion with twice the amount of free hydrochloric acid in the beef tea group There was no apparent difference in the incidence of complications

**Mucin**.—Fogelson (*loc cit*) has introduced gastric mucin for neutralization of gastric acidity It was found that 1

Gm (15 grains) of powdered mucin obtained from hogs' stomachs would neutralize about 15 cc ( $\frac{1}{2}$  ounce) of 0.5 per cent hydrochloric acid Dogs with Pavlov pouches were given 2 ounces (60 cc) of mucin into the stomach and 1 mgm ( $\frac{1}{65}$  grain) of **histamin** were administered In spite of ample secretion in the pouch, no free acid was obtained from the stomach Stimulation of secretion as is seen in alkali therapy did not occur with mucin

Twelve patients with clinical and x-ray findings of duodenal ulcer were treated with the usual bland diet One ounce (30 cc) of mucin was given with each meal and 20 to 40 grains (1.3 to 2.6 Gm) in tablet form every hour All were relieved of subjective symptoms within 3 days

The effect of neutralization with mucin on the production of experimental ulcers has been shown by Kim and Ivy (*loc cit*) It had been previously demonstrated that peptic ulcers developed in about 60 per cent of dogs with permanent biliary fistulas Such fistulas were produced in 27 dogs, 17 of which were then given 15 Gm ( $\frac{1}{2}$  ounce) of mucin with their meals twice daily, while 10 controls received only the regular diet Six of the controls developed ulcers, while none were found in the mucin-fed series of 17 dogs

**Sodium Malate**.—Another method of reducing gastric acidity has been proposed by J C Krantz, Jr, and A A Silver (Ann Int. Med 4 1441 (May) 1931) They found that sodium malate increased the pH with only a slight increase in the total titratable acidity and with an absolute decrease in the total volume of secretion. Nine patients were tested by gastric analysis following the usual bread and water meal A second analysis was done

after adding 6 Gm ( $1\frac{1}{2}$  drams) of sodium malate to the meal. The average pH after the usual meal was 1.6 per cent and after sodium malate 3.77—a definite decrease in acidity. The suggestion was made by these investigators that sodium malate be used instead of sodium chloride in patients with hyperchlorhydria.

**Effect of Tobacco.**—The effect of tobacco upon gastric function was studied by I. Gray (Ann Int Med 3:267 (Sept) 1929) in 300 functional and 100 gastric cases. In the functional group, including patients with pyrosis, duodenal ulcer syndrome, gastroduodenal symptoms and gastritis symptoms, all were relieved upon stopping or curtailing the use of tobacco. In the organic disease group it was found that tobacco increased gastric secretion in the majority, and many were not relieved of symptoms until tobacco was eliminated.

**Diet.**—The principle of producing fine, easily digestible curds by adding acid to milk has been applied to ulcer therapy by R. C. Blankenship and W. H. Oatway, Jr (Ann Int Med 4:1257 (Apr) 1931). Orange juice was found not to increase gastric acidity nor gastric pain. It inhibits hunger contractions, has a slight laxative effect and increases carbohydrate intake, as well as offering a source of vitamins. Orange juice, sodium citrate, citric acid, and tomato juice were tested as to the type of curd formed. Orange juice produced the softest and finest curd. These writers suggest the following formula for use in peptic ulcer: Milk, 24 ounces (720 cc), cream, 8 ounces (240 cc); orange juice, 10 ounces (300 cc), and sugar, 20 Gm (5 drams). Feedings of 6 ounces (180 cc) are given every 2 hours from 8 A.M. to 8 P.M. This program provides 1205 calories distributed

as follows: protein 32 Gm (1 ounce), fat 77 Gm ( $2\frac{3}{4}$  ounces), carbohydrate 96 Gm (3 ounces).

In a review of the various dietary procedures in use for peptic ulcer, there appear to be 4 food principles common to all.

The first requirement is that the food should be soft and bland, in order to be neither chemically nor mechanically irritating to the mucosa. This principle is supported by the work of G. B. Fauley and A. C. Ivy (Arch Inter Med 46:524 (Sept) 1930), which indicated that the consistency of the diet had a direct bearing upon the ulcer. Observations were made as to the manner in which mechanical factors were able to delay the healing of an acute lesion of the gastric mucosa by making it more irritable and susceptible to bleeding. Thus conclusions may be drawn that a diet consisting of soft foods may facilitate in the healing.

Secondly, all foods should be easily digestible and be of a type and consistency which may be quickly worked upon by the digestive juices. In this way, digestion is aided and the possibility of food fermentation in the stomach reduced.

Thirdly, the quantity of food eaten at one time should be small, but feedings should be more frequent, varying from hourly nourishment to a routine of 3 small meals a day, supplemented with additional nourishments.

Lastly, the standard of food constituents in the diet, such as the carbohydrate, protein, fat, and especially vitamins and minerals, must conform favorably with those of the optimum requirement. This applies particularly to the convalescent diet, which may extend over an indefinite period of time. Consequently, the patient must be protected from the vari-

ous conditions, such as lack of appetite, nutritional anemia and others which are very likely to develop if a prolonged deficiency in the diet continues. This last requirement, however, is not expected to be met by the initial diets used during the acute stages of ulcer, such as the Sippy or the modified Sippy routine as outlined here, which includes 3 ounces (90 c c) of 20 per cent cream or equal parts of milk and 40 per cent cream, served every hour from 7 A M to 7 P M (13 feedings)

The following schedule is taken from the Tentative Diet Manual of the University of Michigan Hospital

Day 1 3 oz (90 c c) cream, 20 per cent, every hour, 7 A M through 7 P M

Day 2 Same as Day 1, plus  
10 A M—1 egg \*

Day 3 Same as Day 1, plus  
10 A M—1 egg  
4 P M—cereal \*\*

Day 4 Same as day 1, plus  
10 A M—1 egg  
4 P M—cereal  
6 P M—1 egg

Day 5 Same as Day 1, plus  
8 A M—cereal  
10 A M—1 egg  
4 P M—cereal  
6 P M—1 egg

Day 6 Same as Day 1, plus  
8 A M—cereal  
10 A M—1 egg  
2 P M—1 egg  
4 P M—cereal  
6 P M—1 egg, dessert,† or soup ‡

Day 7 Same as Day 1, plus  
8 A M—cereal.  
10 A M—1 egg  
12 M —cereal  
2 P M—1 egg  
4 P M—cereal  
6 P M—1 egg, dessert, or soup

\* Egg—soft-cooked or poached.

\*\* Cereal—cream of wheat, farina, strained oatmeal, or rice

† Dessert—custard, junket, jello, corn-starch, rice, tapioca and bread pudding

‡ Soup—strained cream of vegetable soup.

Sugar and salt may be given in moderation

Toast, day-old bread, crackers, jelly and cottage or cream cheese may be added on the seventh day

With this diet, which may be maintained from 1 to 3 weeks, the alkaline powders are given every hour, midway between feedings, from 7 30 A M to 9 30 P M. One of these powders (No 1) contained 0.6 Gm (10 grains) of magnesium oxide and 0.6 Gm (10 grains) of sodium bicarbonate. The other powder (No 2) contained 0.6 Gm (10 grains) of calcium carbonate and 2.0 Gm (30 grains) of sodium bicarbonate.

During the acute stages of peptic ulcer, the nutritional adequacy of the diet, in all respects, is not of major importance, nor are the food deficiencies continued for any appreciable length of time, but the convalescent and discharge ulcer diets should always be open to criticism if their protective standards are below normal, which very often is found to be the case when they consist chiefly of milk, cream, eggs, white bread or toast, refined cereals and desserts made from the same. These foods, answering the first requirements, are soft, bland and easily digested, and will meet the caloric, carbohydrate, protein and fat demands. Vitamine A and the calcium and phosphorus content are satisfactory when 1 to 2 quarts (1000 to 2000 c c) of milk a day form the basis of the diet, but, due to lack of variety and the refined state of the remaining foods, iron, an important mineral in protection against nutritional anemia, is usually below the Sherman standard of 15 mg. daily. Very little provision, other than what the milk provides, has been made for vitamine B, the lack of which produces loss of appetite, weight and vigor, also an impairment of the digestive processes, while vitamine C, required for normal tooth maintenance and also protection against loss of weight, appetite and fatigue, is prac-

tically absent, due to the lack of fruits and vegetables

In October, 1931, at the American Dietetic Convention, a list of protective foods was devised by a committee who

had made a study on the "Nutritional Adequacy of the Convalescent Ulcer Diet" This particular list averages 2500 calories a day and includes the following

Whole milk (as a beverage)	7 qts, or 1 qt daily
Cream (20 per cent butter fat)	1 qt, or ½ pt daily
Butter . . .	7 oz, or 1 oz daily
Eggs (yolks particularly)	14 oz, or 2 oz daily
Orange juice (strained)	1 qt, or 4 oz daily
Other fruit juices, such as tomato and unsweetened pineapple	10 oz, or 2½ oz serving 4 days per week
Fresh fruit, stewed and sieved .	5 oz, or 2½ oz 2 days per week
Canned and dried fruits, stewed and sieved	16 oz, or 3 oz 5 days per week
Highly colored vegetables (8 vegetables averaged) .	30 oz, or one 5 oz serving 6 days per week
Cream soup made with one-half sieved vegetable pulp .	48 oz, or 8 oz serving 6 days per week
Irish potatoes (cooked weight)	25 oz, or 3 oz serving daily
Meat (chicken, veal, lamb, scraped beef, boiled or broiled)	18 oz, or 3 oz serving 6 days per week
White fish	7 oz, or 3 oz serving 2 days per week
Bacon (thin)	6 strips, or 3 strips 2 days per week
Cottage cheese	1 cup, or ½ cup 3 days per week
Cereals (cooked, strained)	28 oz, or 4 oz. serving daily
Toast (3 slices from fine graham flour)	19 slices, or 2½ slices daily
Custards and tapioca pudding, etc	6 servings

Foods which contribute little but calories, are not included here as these may be adjusted to the needs of the individual

Two other dietaries taken from the Tentative Diet Manual of the University Hospital of Michigan, "The Initial Ulcer Discharge Diet" and "Final Ulcer Discharge Diet," will meet the optimum standards of nutrition, and are outlined as follows

INITIAL ULCER DISCHARGE DIET  
Tentative Diet Manual,  
University Hospital of Michigan.

*Characteristics.*

- 1 Three meals with 3 supplementary feedings are given
- 2 Meals are limited to 450 Gm (15 oz)

*Foods included*

Beverages made with equal parts milk and 20 per cent. cream milk and cream, malted milk, cocoa, egg-nog  
Soups All strained cream of vegetable soups

Breads Day-old white bread, toast, zwieback, or white crackers  
Eggs Coddled, poached, raw, or soft-cooked  
Cereals Cream of wheat, farina, hominy, strained oatmeal, or pottijohns  
Fruits Apple-sauce, baked apple without skin, puréed canned or stewed peaches, pears, apricots, or prunes  
Vegetables Puréed asparagus, carrots, corn, peas, pumpkin, spinach, squash  
Potato or substitute Mashed, baked or creamed potato, rice, macaroni, noodles, or spaghetti  
Meats Stewed chicken, boiled or creamed fresh fish, broiled scraped beef, ground liver, cottage or cream cheese  
Desserts Custard, fruit whips, jello, junket, tapioca, cornstarch, rice or bread puddings, plain ice cream if eaten slowly.  
Salt Use sparingly  
Very hot and very cold foods—if eaten slowly



*Avoid*

- 1 Highly seasoned foods and sauces, catsup, horseradish, mustard, vinegar, and condiments
- 2 Acid foods, as grapefruit, oranges, tomatoes
- 3 Meat soups and gravies
- 4 Very sweet foods, as cakes, candies, syrups
- 5 Tea and coffee

*Breakfast*

SAMPLE MENU

- 7 00 A M Fruit,  $\frac{1}{4}$  cup  
Cereal,  $\frac{1}{2}$  cup  
Toast, 1 slice  
Butter, 1 square  
Egg, 1  
Beverage, 1 glass  
Sugar, 2 teaspoonfuls
- 9 30 A M Beverage, 1 glass  
Crackers, 4

*Dinner*

- 12 00 M Meat or egg, 2 ounces  
Potato or substitute,  $\frac{1}{3}$  cup  
Vegetable purée,  $\frac{1}{4}$  cup  
Dessert,  $\frac{1}{4}$  cup  
Beverage, 1 glass  
Butter, 1 square
- 2 30 P M Beverage, 1 glass  
Crackers, 4

*Supper*

- 5 00 P M Cream soup,  $\frac{1}{2}$  cup  
Crackers, 4  
Egg or cottage cheese,  $\frac{1}{4}$  cup  
Bread, 1 slice  
Butter, 1 square  
Beverage, 1 glass
- 7 30 P M Beverage, 1 glass  
Crackers, 4

*Note* The above menu furnishes approximately 75 Gm ( $2\frac{1}{2}$  ounces) of protein and 3000 calories

FINAL ULCER DISCHARGE DIET

Tentative Diet Manual,  
University Hospital of Michigan

*Characteristics*

- 1 Three meals with 3 supplementary feedings are given
- 2 Foods containing coarse fiber and highly seasoned foods are avoided

*Foods included*

All foods in Initial Ulcer Discharge Diet with the following additions

Beverages Weak coffee or tea, postum, kaffee hag

Bread Rye

Eggs Any way except fried

Cereals Any dry cereal except those containing bran

Fruits Ripe or baked bananas, canned peaches, pears and peeled apricots, other fruits may be strained and used occasionally

Vegetables Puréed tomato, cauliflower, celery, string beans, young beets, mashed squash, carrots and sweet potatoes, shredded tender lettuce occasionally, raw tomato without skin or seeds

Meats Chicken, creamed or baked or boiled, fish (fresh or canned), creamed, baked, or boiled, broiled steaks or lamb chops, well-done, roast lamb and beef, well-done, ground beef, oysters or sweetbreads, stewed, creamed, or escalloped, liver, baked, broiled, or creamed

Desserts Sponge, angel-food, or plain cake and sugar cookies

Salads Use any of allowed foods with very mild dressing

Salt Use sparingly

Very hot and very cold foods—if eaten slowly.

*Avoid*

- 1 Highly seasoned foods and sauces, catsup, horseradish, mustard, vinegar, and condiments
- 2 Cabbage, onions, peppers, radishes, turnips, and pickles
- 3 Meat soups and gravies
- 4 Corned beef, frankfurters and sausages
- 5 Fried foods, hot breads and pastries
- 6 Nuts
- 7 Overeating

SAMPLE MENU

*Breakfast*

- 7 00 A M Fruit,  $\frac{1}{3}$  cup  
Cereal,  $\frac{1}{2}$  cup  
Egg, 1  
Toast, 1 slice  
Butter, 1 square  
Milk, 1 glass  
Cream, 2 ounces  
Sugar, 2 teaspoonfuls  
Tea or coffee if desired, 1 cup.
- 9 30 A M Beverage, 1 glass.

*Dinner*

12 00 M Cream soup,  $\frac{1}{4}$  cup  
Meat, 2 ounces  
Potato, 1 medium-size  
Vegetable,  $\frac{1}{2}$  cup  
Bread, 1 slice  
Butter, 1 square  
Dessert,  $\frac{1}{3}$  cup  
Beverage, 1 glass  
Cream, 1 ounce  
Sugar, 1 teaspoonful  
Tea or coffee if desired, 1 cup  
2 30 P M Beverage, 1 glass

*Supper*

5 00 P M Cream soup, 1 cup, or  
Milk toast,  $\frac{1}{2}$  slice, 1 cup  
milk, or  
Potato or substitute, 1 serving  
Egg, 1  
Bread, 1 slice  
Butter, 1 square  
Fruit,  $\frac{1}{3}$  cup  
Beverage, 1 glass  
7 30 P M Beverage, 1 glass

**ULTRAVIOLET LIGHT.—  
ADMINISTRATION AND DOSE.**

—The amount of ultraviolet radiation should be gaged by the character of the clinical response to 1 erythema unit of radiation, according to G. J. Warnshuis (Arch Physical Therapy 11 532 (Oct) 1930), and subsequent increase in dosage should be governed by the degree of skin reaction. He feels that it can be increased gradually to a maximum of 5 to 8 erythema doses but that 2 or 3 days should elapse between the exposures. In most cases with symptoms of vitamin deficiency the treatment will fail to be of benefit after about a month's time and should be interrupted until indications of a relapse appear.

In the opinion of J. W. M. Bunker (New England J Med 202:1229 (June 26) 1930), ultraviolet light is an extremely dangerous agent when not used by an experienced worker. In no case should a layman conduct treatment on himself, since severe burning may

result. He states that even today very little is known about the exact amount of ultraviolet light obtained from the various lamps used and that only an expert who has made a careful study of the situation can control the dosage given.

**PHYSIOLOGICAL ACTION.—**

In experiments conducted by J. Skursky (Wien klin. Wchnschr 42 1351 (Oct 17) 1929) on inflammatory exudates from the pleura, the abdomen and the joints, the exudates inoculated with cultures of anthrax were found to have bactericidal power. He found that this bactericidal power was increased following irradiation for 15 minutes at a distance of 30 cm, but that the same does not hold true for the bactericidal powers against colon bacilli, staphylococci and streptococci. Tests on noninflammatory exudates do not show bactericidal power either before or after irradiation.

O. Winterstein (Beitr z klin Chir 151 203 (Dec 27) 1930) attempted to use ultraviolet irradiation on surgical wounds, with the theory that it would produce a clean wound and thus facilitate healing. He found, however, that very little was to be gained by this procedure, as a bactericidal effect and stimulation of cell division could not be produced at the same time. In his endeavor to ascertain whether or not the ultraviolet ray was suitable for use as a sterilizing agent, Winterstein studied the effect on various types of bacteria. In many cases growth could be retarded in new cultures with a 30-second irradiation and the bacilli destroyed in from 5 to 20 minutes. Six-hour cultures of the same organisms showed an increased period of irradiation to be necessary both for inhibition and destruction of the organisms. Some organisms, *i e*, tubercle bacilli and anthrax bacilli, were

impaired in growth, but not destroyed after a 60-minute irradiation. He concluded, therefore, that ultraviolet radiation is not a proper sterilizing agent.

A series of studies were made by J. Chapman and M. Hardy (Am J Hyg 11:404 (Mar) 1930) on the effect of ultraviolet radiation on resistance to infection. In only one case were they able to prove any mitigating influence brought about by irradiation following subcutaneous implantation of *Bacillus leptisepticum*. They consider that sufficient dosage can not be tolerated to warrant the use of ultraviolet radiation.

Both normal and syphilitic rabbits were subjected to ultraviolet irradiation by A. R. Harnes (J Exper Med 52:253 (Aug) 1930) at regular intervals. He found that those irradiated increased in weight more rapidly than the controls. However, this increase in growth was not maintained for long. The irradiated animals were found to be more susceptible to pneumonic infection than control animals and he decided that under certain conditions ultraviolet irradiation was detrimental rather than beneficial.

A study was made by G. Rosenkranz (Klin Wchnschr 10:1022 (May 30) 1931) of the histological changes in the thyroids of rabbits and cattle exposed to skyshine and sunshine, comparing them with those of animals kept in the dark. He found proliferation of parenchyma, reduction in the number of follicles and a reduced colloid content if the animals were kept in the dark, but this did not occur if they were being exposed to sunlight at the time they received ultraviolet irradiation. These changes were found to be most marked in young animals.

A. F. Hess and P. E. Smith (Am J Dis Child 41:775 (Apr.) 1931) re-

port the effects of irradiation on 2 series of rats, male and female, all being litter mates. Some were treated with viosterol in excessive amounts and some with irradiation, in an effort to determine whether or not prolonged and intensive irradiation or large doses of viosterol would have a deleterious effect on the animals. It was found that the growth of animals subjected to these conditions was as good as that of the controls and no difference between the groups was noted at necropsy as regards the endocrine glands.

P. V. Netchaeva (Kazansky Med J 26:143 (Feb) 1930) found that when children with peritonitis, rickets, anemia, tetany, spondylitis and other diseases were exposed to ultraviolet rays, there was a marked increase in hemoglobin and in the number of erythrocytes and leukocytes and a disproportionate increase in the number of eosinophils.

The effect of ultraviolet radiation on sea-urchin eggs was studied by L. V. Heilbrunn (Proc Physiol Soc Phila (Mar 17) 1930, Am J Med Sc 179:730 (May) 1930), who found that exposure to ultraviolet light produced a marked increase in viscosity of the protoplasm, but that this radiation was effective only in the presence of calcium.

From an investigation of the action of ultraviolet irradiation on milk in liquid and powdered form, G. L. Supplee and O. D. Dow (Am J Dis Child 41:1353 (June) 1931) found that under conditions which imparted marked antirachitic properties the antiscorbutic vitamin showed a slight degree of destruction in fluid milk, but under the same conditions there was no destruction of vitamin C in dry milk.

**INDICATIONS.**—In commenting on the use of ultraviolet rays in skin diseases, A. E. Schiller (Radiology 14

sodium hydroxide in a water bath for 5 minutes. The expense of the glycophotometer is much less than a polarimeter and no preliminary preparation of the urine is required. It is also preferable to the fermentation apparatus with which 6 hours are required for determination of the urinary sugar.

Samarin and Myasnikov (*Therapeutische Archiv* 7 799, 1929) state that the *fluorescence method* of measuring the *bile acid content* of the urine has proven to be of value because of its specificity and because the bile acid content of the 24-hour specimen may be examined. Bile acids, according to the authors, are present in an unimportant amount in the urine of normal individuals.

### URINARY INCONTINENCE.

See ENURESIS.

### URINARY RETENTION.—

**ETIOLOGY.**—In the opinion of E. G. Dragonas (*J. d'urologie* 28 341 (Oct) 1929), many cases of retention of the urine are caused by the physiological phenomena exaggerated in one direction or another, there is no pathologic index. In support of this theory, the author cites the cases of prostatectomy in which there is complete recovery of urinary function following the release of the obstruction. He believes the bladder had simply been in a state of inertia before the operation and as soon as the prostate was removed, it regained its normal function.

H. J. McCurrich (*Brit. M. J.* 1:192 (Feb 1) 1930) gives an excellent description of retention of urine. The causes he enumerates as pinhole meatus, phimosis, a congenital fold in the posterior urethra, acute urethritis, prostatitis, abscess, reflex spasm from inflammation in an adjacent organ, trauma,

overdistention, hysteria, stone, stricture, tabes dorsalis, hypertrophic prostate, atony, vaginitis, urethritis, displacement or enlargement of the uterus, prolapse of the urethra, caruncle and nervous disease.

**DIAGNOSIS.**—Retention with an overflow is sometimes mistaken for incontinence and complete retention for suppression, according to McCurrich (*loc cit*). A catheter will solve the differential diagnosis. In partial retention, the amount of residual urine will be determined by the degree of obstruction and if the obstruction is at the neck of the bladder, there will be an overflow when the intravesical pressure reaches a certain point. Any obstruction to the outflow of urine below the bladder will result in trabeculation and dilatation of the ureters and the pelvis, with destruction of the tissue and also the renal function.

**TREATMENT.**—The futility of urinary antiseptics in cases where urinary stasis is present is strikingly pointed out by E. Jaeggy (*Rev. méd. de la Suisse Rom.* 50 561 (Aug. 25) 1930). Because of the metastatic character of the infection, the author believes the source of the infection should always be given first consideration. He believes the actual urinary acidity should be tested daily by the use of **phenolphthalein neutral red** or **methyl red**. The reaction of the urine may be changed at any time to combat the bacteria present. **Methenamine**, for example, acts only in an acid urine and with it acid sodium phosphate is usually given, and its presence will liberate formaldehyde. Heavy metals, especially **silver** and **gold**, in colloidal form are more efficacious than iodized metallic salts. **Arsphenamine** is particularly valuable in staphylococcal infections.

**Mercurochrome** is more powerful than any other antiseptic, but its danger lies in the mercury and it cannot for that reason be administered by mouth.

One of the most common and annoying complications of surgery in an otherwise normal postoperative course is the inability of the patient to empty the bladder. The danger of the use of a catheter under proper aseptic precautions has probably been overemphasized, but its elimination is to be desired especially in the apprehensive type of patient. In a small series of patients, E. Kotilors (*Zentralbl f Gynak* 54 2530 (Oct 4) 1930) has found that the rectal infusion of 50 cc ( $1\frac{2}{3}$  ounces) of a 2 per cent **novocaine solution** will accomplish the desired result in 84 per cent of the cases. It cannot be expected that the bladder will be found distended in those individuals who have been markedly dehydrated before operation and the rectum should be well emptied before any attempt is made to administer the novocaine solution.

R. Gutierrez (*Surg Gynec Obst* 50 441 (Feb) 1930) claims that the **indwelling catheter** is of value in urinary surgery, not only for diagnosis and treatment, but as a convenience during and after the operation. It is essential that the catheter serve the purpose of promoting drainage, relieving pain and correcting infection. A double catheter has proven quite satisfactory in the hands of the author in the treatment of "renal colic," ureteral calculi, pyelitis and pyelonephritis, the so-called iodopathic hematuria, urinary stasis with or without infection and in calculous anuria. The technic of the indwelling ureteral catheter according to the author is merely that of cystoscopy and catheterization of the ureters.

The treatment of the congenital

lesions is obvious. In retention due to spasm or inflammation, the **cause must be removed**. McCurich (*loc cit*) recommends the use of **hot baths** and **hot applications** and the administration of **morphine**, **atropine** and **calcium chloride** may be indicated. *Strictures* should be treated under either **local or spinal anesthesia** and extreme care must be taken to prevent the formation of a false passage. The author prefers **small heavy sounds** to the gum-elastic bougies. He states that if the passage is impossible, drainage may be obtained suprapubically with a **very fine needle**. In the treatment of strictures not suitable for dilatation, resilient strictures and strictures that bleed easily, and in the treatment of periurethral abscess, **internal urethrotomy** is indicated.

For catheterizing the patient with an enlarged prostate, the author prefers **Tieman's catheter**. This is made of soft rubber with a solid rubber tip which is turned up at the end so that it will ride over the prostate. Rectal palpation, urinalysis and cystoscopic examination are also required for the diagnosis of prostatic hypertrophy.

**UROBILINURIA.**—In experiments with 11 patients with heart disease with decompensation and 13 patients without cardiac disorders, E. Adlercreutz (*Finska laka sällsk handl* 72.974 (Dec) 1930) found that the ingestion of 1 liter (quart) of water, followed by a bending exercise, repeated 25 times, resulted in a "pathologic" urobilinuria in those patients having cardiac disorders. Reference is made to the recent studies revealing the importance of the liver in the water metabolism of the body, and the writer queries whether this partial function of the liver

is especially called upon in these cases with heart disease, because there is, after all, a latent cardiac insufficiency

E Forsgren (Hygiea 93 337 (May 15) 1931) reports his studies on the daily variations in urobilinuria. He believes that postalimentary increase of urobilin in the urine is not a perfectly regular phenomenon in healthy individuals. In addition to the variations following the ingestion of food, the author considers that urobilinuria presents variations to a certain degree independent of alimentary influences. The urobilin in the urine usually increases and reaches a maximum during the day, often decreasing in the evening in spite of the ingestion of food, and reaches a minimum during the night, sometimes disappearing entirely to reappear in the morning even on a fasting stomach. The author believes these daily variations in urobilinuria will recall to mind the daily variations in the secretion of bile and a connection between the urobilinuria and the rhythmic liver function seems quite probable.

**UROGRAPHY.**—The development of *uroselectan* as a contrast substance for urologic work was the result of research in the direction of obtaining a satisfactory contrast medium for cholecystography, according to I S Hirsch (Radiology 15:480 (Oct) 1930). The preparation perfected by Bintz and Rath is nontoxic, soluble in water and is excreted in sufficient concentration to give good x-ray contrast. The iodine content of the preparation is 42 per cent. The method permits (1) visualization of the urinary tract, (2) study of the physiology of the urinary tract, and (3) the determination of the kidney function.

According to Hirsch, the *indications*

for intravenous urography are (1) cases in which anatomical or pathological obstacles exist for cystoscopy, ureteral catheterization or instrumental pyelography, (2) those cases which have a ureteral obstruction preventing the upward flow from the bladder of any contrast medium, and (3) cases where instrumental pyelography is definitely contraindicated or impossible.

A Randall (Ann Surg 93 1202 (June) 1931) relates that pyelography by means of *iopax* is an entirely physiological procedure and that it outlines the urinary tract without artefacts, providing for the study of the dynamics of the entire system. Good pictures are not to be desired, as they are an indication of disturbed function of some part of the tract. Failure of excretion indicates lack of unilateral or bilateral function. The author points out the fact that the examiner should not hesitate to fall back upon the more tried and understood methods, *ie*, ureteral catheterization, differential functional tests and instrumental pyelography. To the author the most important adjunct of this procedure will be the establishment of a close cooperation between the roentgenologist on the physical side and the urologist on the clinical side. The ease with which the method may be employed and the difficulties arising from the interpretation of the results will cause a large amount of confusion and many needless operations, besides, the proper procedure may be denied the patient as a result of ignorance if this cooperation does not exist.

A. L. Wolbarst and I S Hirsch (M J and Rec 132 1 (July 2) 1930) report that iodism has never been noted following the use of *uroselectan*. They describe the technic as follows: A 40-gram ( $1\frac{1}{3}$  ounce) package of the



*uroselectan* is dissolved in 80 c c (2 $\frac{3}{4}$  ounces) of heated double distilled water. The solution is then twice filtered, sterilized by heating for 20 minutes over a steam bath, cooled and injected intravenously in 2 injections separated by an interval of from 2 to 5 minutes. The renal pelvis becomes visible 5 minutes after the injection, but the visualization of the entire urinary tract requires from 15 to 20 minutes.

Particular stress is placed by R. V. Cooke (Lancet 2 686 (Sept 27) 1930) on the value of intravenous urography in pediatric work, in severe **cystitis**, especially **tuberculous**, in cases of profuse **hematuria**, **ureteral stricture** or **enlarged prostate**, and in the subsequent examination of kidneys whose ureters have been previously transplanted.

The excretion rate may be measured by determining the entire output of urine or, more simply, by following the changes in the specific gravity of the urine. Attention is called to the fact that impairment of the function of the kidney may be only temporary and for this reason one examination by the method of intravenous urography may be misinterpreted.

A series of 85 cases of adults and children of both sexes has been compiled by H. L. Kietschmer (Surg Gynec Obst 51 404 (Sept) 1930), in which the use of *uroselectan* was found to be nonirritating and nontoxic. There were very few local reactions and no general reactions such as chills or fever.

The congenital anomalies which were easily demonstrated by this method were **bifid pelvis** and **horseshoe kidney**. In a case of solitary **kidney** with a **stone** in the pelvis on one side, no shadow appeared on the other side and cystoscopy and chromocystoscopy failed to reveal a left ureter. The diag-

nosis was verified upon the operating table. In cases of unilateral involvement, the affected side appeared in marked contrast to the normal side. The shadows of all forms of stones in different positions were intensified by the *uroselectan*.

Because of the rapid accumulation of *uroselectan* in the urinary bladder, it is necessary to catheterize the patient when the lower end of the ureter is the site of interest in the study. A very rapid disappearance of ureteral dilatation following the passage of stone and dilatation of strictures may be easily watched by this process. **Neoplasms of the kidneys** are well defined by this method because of the appearance of the deformities which are shown. The author has used the solution in one-half strength for ascending pyelography, as he believes it to be of extreme value in the differentiation of pain in the upper right quadrant and in the region of the spleen.

**UTERUS.—CERVICAL CARCINOMA.**—K. Bartlett and G. van S. Smith (Surg Gynec Obst 52 249 (Feb) 1931) present an interesting review of 673 cases of carcinoma of the cervix treated at the Free Hospital for Women by W. P. Graves and F. A. Pemberton in their private practices.

Of 588 patients on whom a family history was available, 104 per cent gave a history of malignant disease. In this series 107 per cent of the patients gave a history of no pregnancy. An additional 49 per cent gave a history of abortions or miscarriages but no full-term pregnancy. Routine microscopic examination of curetting and trachelorrhaphy specimens at this hospital has led to the detection of 16 early cases of carcinoma of the cervix grossly unsuspected.

Approximately 1700 cervixes were deeply cauterized in this hospital between 1914 and January, 1929. No one of these patients is known to have developed cervical carcinoma.

The incidence of squamous carcinoma exceeded that of adenocarcinoma by a ratio of 7.5 to 1. The operative mortality for complete hysterectomy was 11.2 per cent. Calculating for the years 1902 to 1930, the operative mortality was 6.5 per cent. Contrary to the usual expectation, the results from complete hysterectomy are rather better than those from radiation.

**Etiology.**—A series of 226 cases of known carcinoma of cervix have been compared by F. R. Smith (*Am J Obst and Gynec* 21:18 (Jan) 1931) with 202 normal patients with the hope of finding possible etiologic factors. Parturition with its resulting cervical trauma is a generally accepted factor in cancer of the cervix. These studies show that there are apparently 5 additional possible factors: (a) Length of time between marriage and first delivery, with the suggestion of a possible field for investigation as to contraceptives employed; (b) use of douches with liquor cresolis comp; (c) more than one instrumental delivery; (d) dry labor; (e) untreated cervical lesions with leukorrhea.

One of these 5 possible factors was not present more often in cancer patients than in the control group, but with the presence of 2 or more factors, the inequality in percentages of each group total progressively increased with the increase in number of factors.

**Diagnosis.**—The importance of leukoplakia as a *precancerous* condition is emphasized by F. Emmert (*J A M A* 97:1684 (Dec 5) 1931). A leukoplakia is a disorder of the mucous mem-

brane, characterized by an increased formation of keratin in the superficial layers of the squamous epithelium and a marked hyperplasia of all other constituents of the mucous membranes, until the latter closely resembles the epidermis in microscopic appearance. These changes result in the production of bluish, pearly or grayish white plaques, which are either level with the surrounding mucosa or slightly raised, if the hyperplastic process has been excessive. Leukoplakia, although most often found on the oral and vulvar mucosa, is sometimes found in higher parts of the vagina and on the cervix. The author uses the colposcope, designed by Hinselmann, of Germany, which enables the examiner to inspect the cervix most thoroughly. The colposcope consists of a pair of binoculars mounted on an adjustable upright. When the cervix is exposed in a speculum, the surface of the vaginal portion can be studied carefully with satisfactory illumination and the magnification renders even the most minute lesion visible.

According to B. Whitehouse (*Lancet* 1:1 (Jan 3) 1931), the most important diagnostic sign in cancer of the uterus is the hemorrhage occurring as a direct result of coitus. Occasionally a blood stained discharge or slight actual hemorrhage follows coitus when the cervix is the seat of an extensive erosion and eversion, or contains a small polyp. A severe bleeding associated with coitus is, however, nearly always evidence that cervical carcinoma exists and calls for thorough study.

A. G. Issachanow (*Zentralb f Gynak.* 55:1215 (Mar. 28) 1931) reports his experience with the *Shiller method* for the early diagnosis of cervical carcinoma which is a valuable ad-

junct to the histologic method. Normal tissues take the iodine stain, whereas diseased tissues remain iodine negative, due to a deficiency in the glycogen content of atypical proliferating epithelial cells. The author orders a vaginal douche, following which a speculum is inserted and the cervix is dried with cotton and painted with 5 per cent tincture of iodine. The major portion of the cervix will be stained brown but in the suspicious cases there will be clear points (iodine negative) within this dark brown field. This part is either curetted away or excised and examined histologically. Early cancer, he claims, can thus be detected in more than twice as many cases as by the simple biopsy.

**Prognosis.**—A study has been made by W. L. McNamara (J. Lab. and Clin. Med. 15:976 (July) 1930) of 294 patients with carcinoma of the cervix with the viewpoint of determining the relation of histology to prognosis.

Microscopic examination is one of the most valuable aids in this study of a prognostic index. He divides the squamous-cell type of cancer into 2 types of malignancy, the "high" and "low."

The high group consists of spindle cells with much chromatin and a small nucleus. They are closely packed, giving the appearance of the ordinary basal-cell carcinoma. This is the highest or most malignant type of cancer found. Along with this squamous cell there is usually a round cell with clear cytoplasm and a very early chromatinized nucleus which never invades the tissues.

The "low" group consists entirely of large even cells which have a tendency toward "pearl" formation. The cells, as a rule, are equal in size and do not infiltrate.

**Treatment.**—Some of the refinements which should accompany radium irradiation of cancer of the cervix are pointed out by H. Swanberg (Radiology 15:290 (Aug.) 1930). Every case of advanced cancer of the cervix, he claims, should receive external irradiation, and if this is given by high-voltage x-rays, it should precede the internal radium therapy.

No patient should receive radium unless the local infection which so frequently accompanies cervical cancer is controlled by suitable douches.

After a week of preliminary treatment, the cervical canal is gradually dilated and the length of the uterine canal noted. The patient returns to bed where her temperature is taken at frequent intervals. If the uterine canal is patent the principal internal radium treatment should be given, as the best results are obtained by placing radium the entire length of the canal. If the canal is not patent, preliminary radium treatments to open it, or cervical amputation by electrothermic measures, are essential before the principal internal radium treatment is given.

H. H. Bowring and R. E. Fricke (Minnesota Med. 14:237 (Mar.) 1931) describe the present method of irradiation treatment of cancer of the cervix as employed at The Mayo Clinic. Intensive fractional dosage is used, a massive dose being applied over a 2 to 3 week period. The radium is used in 8 applications and is applied vaginally, in the cervix and intrauterinely, followed by 1 to 3 courses of x-ray treatment.

The usual radium applicator employed is the 50 mg. universal tube filtered through 1.5 mm. of monel metal and shielded by 2 mm. of lead and 1 cm. of Para rubber or a tube containing 50 millicuries of radon enclosed in 0.5 mm.

of silver and 1 mm of brass. This is left *in situ* for 12 to 14 hours. The entire length of the cervical canal and uterus is treated, applying 2 treatments to each 2.5 cm of canal. The vaginal applications are made to the face of the cervix and in each fornix.

In large cauliflower masses radium in platinum needles is implanted, applications being made with the patient in the knee-chest position.

Seventy-five per cent of the early cases treated obtained a 5-year cure, while 61.5 per cent of the borderline cases, 21.5 per cent of the inoperable, and 24.8 per cent of those with modified lesions obtained 5-year cures. The hospital mortality over a 10-year period has been 1 per cent.

P. Begouin (Bordeaux chir. (Apr. 1) 1930) reviews a very interesting series of 75 Wertheim operations for cancer of the cervix performed between 1904 and 1918, with 6 deaths, or 8 per cent mortality. Fifty per cent of the patients traced from 10 to 25 years were living and well, 5 patients were alive more than 20 years, 5 more than 15 years, 5 more than 12 years and 5 more than 10 years.

The operations were all radical abdominal hysterectomies with dissection of the ureters and vaginal drainage, but the iliac vessels were left unligated.

A comparison of these European statistics with the results obtained in this country by radium therapy would appear to indicate that the mortality following irradiation gives as good results.

**DISPLACEMENTS.—Treatment.**—W. P. Graves and G. V. Smith (Surg. Gynec. Obst. 52:1028 (May) 1931) are enthusiastic advocates of Olshausen's uterine suspension operation and review 3358 cases. This operation was performed in over half of

the cases for the cure of prolapse and procidentia. Of the cases which were followed for more than 2 years, symptomatic cures were obtained in 66.8 per cent, relief was obtained in 27.3 per cent, while in 5.6 per cent the operation was a failure. In 76.9 per cent the uterus was in good position, in 14.2 per cent there was a partial recurrence, and in 8.8 per cent there was a complete recurrence.

Pregnancy occurred 856 times in 489 patients (17.6 per cent of the traced cases) of which 406 had normal deliveries. In 197 of the pregnant patients abortions and miscarriages occurred, while the remainder had a complicated delivery.

In the postnatal follow-up examination, the uterus remained in normal position in 71.4 per cent, a partial recurrence occurred in 12.7 per cent, and a complete recurrence in 15.7 per cent. Only 6 cases of intestinal obstruction occurred.

**FIBROIDS.—Treatment.**—In a discussion of the surgical treatment of uterine fibroids, J. Cohen (South M. J. 23:875 (Oct.) 1930) reports 1000 consecutive cases treated at the Charity Hospital in New Orleans. Among these 695 were operated upon, 86.4 per cent having an abdominal supravaginal hysterectomy, 4.5 per cent an abdominal panhysterectomy, 0.45 per cent a vaginal hysterectomy and the remainder treated conservatively. Sarcoma was found by the pathologist in 1 case and cervical carcinoma in 2. The operative mortality was 4.6 per cent. Syphilis, it was rather conclusively shown, had little influence on mortality, since the incidence of a positive reaction in the entire series was 20.4 per cent, while of those who died, only 16.6 per cent had a positive reaction.

**HEMORRHAGE.—*Etiology.***—C F Fluhmann and D L Morse (Am J Obst and Gynec 21 455 (Apr) 1931) have carried out a most extensive analysis of 1137 cases of abnormal uterine bleeding which occurred in 630 pregnant and 507 nonpregnant women. The patients in the nonpregnant group were classified into 8 distinct categories.

1 Menorrhagia, or profuse or prolonged flow in patients with otherwise normal menses. The sequence of events of the menstrual cycle in the ovaries and endometrium is undisturbed. The most frequent etiologic factor is any condition that interferes with the contractile power of the uterus or results in a hyperemia of the pelvic organs.

2 There is an irregularity in the time factor, the menstrual periods appearing too frequently, or are delayed, or are totally irregular in their occurrence. The main etiologic factor is to be sought in disturbances of ovarian function, which may be of a primary endocrine nature or secondary because of anatomic lesions.

3 (a) Hemorrhage initiated with a menstrual period may continue for a prolonged length of time. In these cases are mainly found lesions intimately connected with the endometrium, such as submucous fibromyomas and endometrial polyp, or definite pathologic changes such as hyperplasia of the endometrium or endometritis.

(b) Continuous bleeding may set in during the stage of endometrial proliferation. The physiologic explanation may be found in a sudden destruction of the corpus luteum due to extension of an inflammatory process.

(c) Bleeding during the endometrial stage of secretion is of unusual occurrence and may be partly due to the

premenstrual hyperemia of the pelvic organs.

4 Hemorrhage may occur in the middle of the menstrual cycle at a time corresponding to the rupture of the Graafian follicle, the so-called ovulation bleeding.

5 A type of hemorrhage characterizing hyperplasia of the endometrium is found when the menstrual periods become progressively more profuse or irregular and end finally in continuous bleeding.

6 Bleeding may occur following a period of amenorrhea in nonpregnant women of the child bearing age, due to (a) hyperplasia of the endometrium, or (b) a traumatic or ulcerative lesion of the uterus following a previous removal or destruction of the ovaries.

7 Hemorrhage may occur at irregular times and without any connection with the events of the menstrual cycle, as a result of traumatic or ulcerative lesions of the cervix or endometrium resulting from new growths or inflammation.

8 Irregular hemorrhage due to the same causes as in group 7 may occur in women past the climacteric. In rare cases, ovarian new growths may also affect the endometrium and produce bleeding.

In a large series of patients with abnormal uterine hemorrhage observed by C F. Fluhman (J A M A 97:694 (Sept 5) 1931), pelvic inflammatory disease accounted for the disorder in 16 per cent of the patients who had not passed the menopause. Abnormal uterine bleeding is found in from 35 to 50 per cent of all patients with acute or chronic salpingitis.

In the present study of 52 patients with pelvic inflammatory disease of gonorrheal origin with associated bleed-

ing, the bleeding manifested itself in 5 ways, *i e*

- 1 Menorrhagia (15 cases)
- 2 Polymenorrhea (15 cases).
- 3 Atypical irregular bleeding (12 cases).
- 4 Continuous bleeding, the onset coinciding with a normal menstrual period (2 cases)
- 5 A period of bleeding, the onset occurring between the eighth and eighteenth days of the cycle

The most important factors concerned in the production of the bleeding are.

1. Interference with normal uterine contractions and the presence of a pelvic hyperemia.
- 2 Inflammatory lesions of the endometrium
- 3 Disturbances of ovarian function induced by chronic perioophoritis and hyperemia or by corpus luteum abscess formation.

**UVEITIS.**—A review of 17 cases previously reported in the literature, has been made by W. R. Parker (Am J. Ophth 14: 577 (July) 1931), who adds 2 new cases of uveitis associated with alopecia, poliosis, vitiligo and deafness. The etiology is obscure. Peters suggested that the uveal tract is first affected and that changes in the other pigmented structures, skin, hair and possibly the pigment in the basilar membrane in the labyrinth, are due to anaphylaxis from the disseminated uveal pigment; Koyanagi believes that all the changes are due to a common source of infection.

The uveitis is always bilateral. Alopecia and poliosis are always present and temporary deafness occurs in half the cases. Vitiligo occurred in 66 per cent. of the reported cases. The Wassermann

reaction was positive in 12 per cent of the patients examined. The resemblance of this form of uveitis to sympathetic ophthalmia is striking, alopecia, poliosis, and deafness having also been observed in the latter conditions.

H. G. Merrill and L. W. Oakes (Am J Ophth 14: 15 (Jan) 1931) tabulate 30 cases of *uveoparotitis* reported in the literature and add a personal case in which the condition was associated with a rash resembling erythema nodosum, the symptoms persisting for 2 years and 10 months. After withdrawal of a pleural effusion which had existed for 1 week the temperature dropped. No evidence of tuberculosis was found.

Iridocyclitis or uveitis, bilateral, painless swelling of the parotid glands, without suppuration, and a low grade fever are the cardinal signs of this rare condition. Treatment is symptomatic and the condition usually resolves spontaneously. X-ray treatment and tuberculin may hasten resolution. The authors conclude that a search for tuberculous foci should be made which, however, is usually unsuccessful. They believe that a specific virus or agent is the etiologic factor.

W. S. Lemon (Am J Ophth 14: 869 (Sept) 1931) discusses the criteria by which the internist determines the etiologic factors of uveitis. *Tuberculosis*, almost certainly secondary to tuberculosis elsewhere, is recognized as one cause of uveitis. He concludes that bacteria either reach the eye or set up an allergic reaction in the eye from a primary focus.

Two cases of uveitis which occurred in young women while under sanatorium care for active pulmonary tuberculosis are reported by W. V. Moore (Am. J. Ophth 14: 596 (July) 1931). In each case the condition cleared up and vision



was restored His review of the literature indicates that tuberculous eye lesions are rarely found among patients with active pulmonary tuberculosis He

concludes that, while ocular *tuberculosis* is probably hematogenous and secondary to a focus elsewhere, the primary lesion is usually slight, quiescent or calcified

## V

**VAGINAL TRICHOMONIASIS.—DIAGNOSIS.**—In order to determine the causative relationship of the trichomonas to obstinate leukorrhea, and especially its influence on the normal vaginal flora and thereby its ultimate bearing on puerperal morbidity, P Brooke Bland, L Goldstein and D H Wenrich (J A M A 96 157 (Jan 17) 1931, Surg Gynec Obst 53 759 (Dec ) 1931) systematically examined the vaginal secretion of 500 consecutive patients registering in the antenatal clinic of the Jefferson Medical College Hospital.

In conducting the technical steps of their investigation an ordinary bivalve speculum, not lubricated, is introduced into the vagina, exposing the cervix and especially the deep concavity in the posterior vaginal fornix The material thus gathered is transferred to a sterile tube containing 2 cc ( $\frac{1}{2}$  dram) of physiologic solution of sodium chloride A drop of the secretion mixed with the saline solution is placed on a clean slide and examined under high magnification for living flagellates The saline secretion mixture is then transferred to a tube containing the culture medium and incubated at 37.5° C (99.5° F).

Many features of the morphology, life history and host parasite relations of trichomonas vaginalis are completely known There is rather general agreement, however, as to the fusiform or pear-shaped body, about twice the size of a leukocyte with free flagella at the

anterior end, an undulating membrane extending backward to near the middle of the body, and an axostyle projecting posteriorly The size varies from 7 to 30 microns in length, with a width usually from one-half to two-thirds the length

In fresh material the living flagellates are exceedingly active, exhibiting the jerky forward motion accompanied by a counter-clockwise rotation on their long axes, that may be seen in most trichomonads On slides fixed with Schaudinn's fluid or other adequate fixative and stained with iron hematoxylin, it usually will be found that the cytoplasm contains many deeply staining granules which often obscure the other internal structures

**Cultivation.**—When cultivation is to be attempted, the media should be prepared in advance For routine work after numerous trials they found that the simplest method that has given a high degree of success is the following. Prepare sterile agar slants (Bacto nutrient agar) and just before inoculation add 10 cc ( $2\frac{1}{2}$  drams) of 70 per cent. Ringer's solution to which Loeffler's dried blood serum has been added in the proportion of 0.3 Gm (5 grains) to 100 cc ( $3\frac{1}{2}$  ounces). After inoculation, tubes are incubated at from 36° to 37° C Examine on the second or third day and make transplants on the third or fourth day, if growth occurs The flagellates will be found in greatest numbers at the bottom of the tubes

**Slide Making.**—Bacteriological methods are not usually satisfactory for trichomonad flagellates. Two other general methods may be employed, *i.e.*, (A) dried smear methods, or (B) wet smear methods.

**A Dried Smear Methods**—(a) Vaginal secretion, diluted with physiological salt solution, is spread in thin films on micro slides and allowed to dry, or (b) a drop of the diluted secretion is placed in the middle of a slide and the drop inverted over a bottle containing 1 or 2 per cent osmic acid, after 20 to 30 seconds exposure to the osmic acid vapor, the drop is spread in a thin smear and allowed to dry. In either case the smears should be made as thin as possible.

Two methods of staining may be followed. (a) Fix films for 5 to 10 minutes in pure methyl alcohol and allow to dry again. Stain 20 to 30 minutes with Giemsa's stain, diluting the stock stain in the proportion of 1 drop to 20 drops of tap water or of neutralized distilled water. Wash in tap water, dry and examine with an oil immersion lens, or mount under a cover glass, using damar resin as a mounting medium. When staining is complete, flush off the stain and examine while still wet under the high dry objective; if the stain is too intense, prolong the washing in tap water. (b) Without previous fixation, the films may be stained with Wright's or Leishman's blood stains in the usual way. Washing in water may have to be prolonged for several minutes to secure the best differentiation.

**B Wet Smear Methods.**—The best fixative is Schaudinn's fluid (dissolve 6 Gm ( $1\frac{1}{2}$  drams) of mercuric bichloride in 100 cc ( $3\frac{1}{3}$  ounces) of distilled water, to this mixture add 50 cc ( $1\frac{2}{3}$  ounces) of 95 per cent or absolute ethyl

alcohol, to 95 parts of this mixture add 5 parts of glacial acetic acid and use). This is best employed at 30° to 40° C (86° to 104° F), but may be used at room temperature. Other standard fixatives, such as Zenker's, sublimate-acetic or Bouin's fluids may be used, but Schaudinn's seems to give the best results.

Vaginal secretion, slightly diluted with saline, is spread in a thin film on a slide and the slide dropped into a jar of fixative before drying can occur. Fixation may be for 10 minutes to several hours. Next place the slides in 50 per cent alcohol for 10 minutes or longer, then 70 per cent alcohol containing a little iodine (Lugol's solution) for 10 minutes or longer, then in clear 70 per cent alcohol, in which they may be kept till ready for staining.

The best staining method is that with iron alum and hematoxylin, but this requires practice to produce satisfactory results. The following program may be followed.

- From 70 per cent alcohol to
- 1 30 per cent alcohol, 1 to 5 minutes
- 2 10 per cent alcohol, 1 to 5 minutes
- 3 Water, 1 to 5 minutes
- 4 4 per cent iron alum, 30 minutes to 24 hours
- 5 Water, 1 to 5 minutes
- 6  $\frac{1}{2}$  per cent hematoxylin (ripened) as long as the time in the iron alum
- 7 Water (rinse)
- 8 Differentiate in 2 per cent iron alum, 1 to 5 minutes. Rinse in water and examine frequently with microscope to note progress of destaining.
- 9 Water (running or frequent changes), 15 minutes
- 10 30 per cent alcohol, 1 to 5 minutes
- 11 70 per cent alcohol, 1 to 5 minutes
- 12 95 per cent alcohol, 5 to 10 minutes
- 13 Absolute alcohol or a clearing solution (alcohol-xylol, carbol-xylol, oil of cloves, etc), 5 to 10 minutes
- 14 Xylol (2 changes), 5 to 10 minutes
- 15 Mount in balsam or damar

When properly handled, this method gives an excellent differentiation of chromatic elements (nucleus, blepharoplast, chromatic granules and the filaments) as staining dark or black against a gray or colorless background. Counter stains, such as eosin, orange G, Bordeaux red or light green may be employed but are not necessary.

After fixation and washing, the slides may be stained with hemalum or with Delafield's hematoxylin, but these are not as satisfactory as the iron alum-hematoxylin method.

The vaginal secretion of the 500 patients studied, revealed the parasite in 118 or in 23.6 per cent. According to race, trichomonas was present in 32, or 13.2 per cent, of 243 white and in 86, or 33.7 per cent, of 257 negro patients. Only 15, or 12.6 per cent, of the patients suffering with vaginal trichomoniasis complained of local symptoms, although almost all experienced an abnormal vaginal discharge.

From their observations, these investigators are inclined to believe that the parasite is pathogenic and is capable of producing a rather characteristic purulent discharge and occasionally a more or less typical type of punctate hyperemic vaginitis.

The relationship of vaginal trichomoniasis to puerperal morbidity was studied in 152 patients. The morbidity rate for both white and negro women suffering with the infection, regardless of the mode of delivery was found considerably higher than in patients free from the parasite, reaching 75 per cent. in white and 41 per cent. in negro patients. To prevent post-partum complications, therefore, ante-natal treatment of the infection is advisable.

**TREATMENT.**—The following treatment is recommended by J. P.

Greenhill (J. A. M. A. 96:1862 (May 30) 1931). The vagina is thoroughly scrubbed with gauze or cotton saturated with tincture of green soap. All the vaginal folds are smoothed out and every part of the mucosa is scrubbed. The vulva and anal region are likewise scrubbed. The scrubbing is persisted in until slight bleeding from the vaginal mucosa is noted.

The soap is washed out with tap water or with bichloride of mercury and the vagina is dried. A vaginal speculum is inserted and hexylresorcinol is instilled into the vagina and on the cervix. A tampon saturated with half or full strength glycerin is then inserted high up into the vaginal vault. A second, dry tampon is inserted to prevent the escape of glycerin on the patient's clothing. Hexylresorcinol is applied to the vulvar and anal regions and the patient is instructed to remove the tampons after 24 hours.

After removal of the tampons, a douche of tincture of green soap is taken. This entire treatment is repeated every second day for at least 3 times, the patient taking a green soap douche on the mornings between treatments. Treatment is continued until hanging drops on 2 successive visits fail to show the trichomonas. After treatment is discontinued the patient takes a 0.5 per cent lactic acid douche for 2 weeks.

To prevent reinfection if the causative organism comes from the rectum, the patient is instructed to be very careful in cleansing the anal region, using a sweeping motion directed away from the vagina and toward the sacrum.

Since recurrences are frequent, especially after a menstrual period, patients should be reexamined immediately before and just after the menstrual period, following the course of treatment.

## VARICELLA (CHICKEN-POX).

—**BLOOD.**—During the past year further observations of the blood picture of varicella patients have been reported. N. Carrara (*Pediatrics* 38:865 (Aug 15) 1930) noted a relative lymphocytosis with a decrease in the polymorphonuclear cells in the blood during the incubation period of the disease, while in the stage of eruption there was a leukopenia with a relative increase of the lymphocytes. During convalescence, the number of white corpuscles increased to the extent of producing a true leukocytosis. The percentage of mononuclear cells (monocytes) increased in the blood of a few patients. The red corpuscles did not vary noticeably in number or morphology throughout the infection.

An unusual pseudoleukemic blood condition occurring in a patient with chicken-pox was reported by D. Goldman (*Am J Dis Child* 40:1282 (Dec) 1930). A few days after the onset of the disease the leukocyte count rose to 81,200 with 86.5 per cent lymphocytes and gradually receded to normal in 3 or 4 weeks' time. The number of erythrocytes remained normal and there was no marked increase in the number of young forms of cells of any type. Attempts to reproduce the condition in the child, first by the injection of typhoid vaccine and later by smallpox vaccination, failed to cause a similar leukocytic response.

**COMPLICATIONS.**—A few complications of chicken-pox have been reported from time to time. J. Zahorsky (*J A M. A.* 94:484 (Feb 15) 1930) observed a child with a *diphtheritic infection of a gangrenous chicken-pox lesion*. The patient died with signs of myocardial failure and peripheral nerve paralysis. The author advocated that **diphtheria antitoxin** be administered

immediately to every patient whose chicken-pox lesions appear gangrenous, rather than awaiting the establishment of the diagnosis of diphtheria.

K. Ochsenius (*Monatschr f Kinderh* 46:127 (Feb) 1930) reported the occurrence of post-chicken-pox *nephritis* in 3 members of the same family.

*Central nervous system complications* of chicken-pox have been observed recently with increasing frequency. Two such patients were described by E. Tramer (*Med Klin* 26:1598 (Oct 24) 1930). On the sixth day after the appearance of the chicken-pox eruption, one child of 7 years developed symptoms which indicated involvement of portions of the medulla and cerebellum. The second child, 3 years of age, had findings resembling those of *poliomyelitis*, which appeared also on the sixth day of her chicken-pox. Both children recovered completely.

A review of the literature revealed the reports of 32 patients with chicken-pox who had had complications of *central nervous system type*. These were collected and summarized by W. R. Brain (*Brit. M J* 1:81 (Jan 17) 1931). All but 2 of the patients were children. Generally, the complication began on the fifth to the twentieth day after the onset of the chicken-pox. In 11 instances, the predominant symptoms indicated involvement of the cerebellum and in 8 of the spinal cord. Tremor was the outstanding symptom in 3 patients, meningeal irritation in 2, choreiform movements in 2, ophthalmoplegia in 2, while 1 patient had diplegia, 1 a hemiplegia and 1 became comatose.

J. A. Chavany and A. Chaignot (*Bull. et mém Soc méd d hôp. de Paris* 47:28 (Jan. 19) 1931) saw a patient who developed symptoms of *vertigo, persistent vomiting* and *brady-*

cardia 4 days after the appearance of a chicken-pox rash. There was no fever, no sign of meningeal irritation and no increase of the number of cells in the spinal fluid. Within 15 days the symptoms had abated and at the end of 3 weeks had disappeared entirely.

The effect of a chicken-pox infection on patients with *tuberculosis* has received considerable attention lately and the general opinion indicates that the former disease frequently activates the tuberculous infection. G. Abraham (Monatschr f Kinderh 46 97 (Feb) 1930) had a patient with chicken-pox who immediately afterwards developed a large lymph gland which was proved to be tuberculous by guinea-pig inoculation.

W. Schwenk (Ztschr f Kinderh 49 686, 1930) observed several children with tuberculosis of the spine who developed *tuberculous meningitis* immediately after attacks of chicken-pox. G. A. Schiavone (Semana méd 2 1495 (Nov 21) 1929) gives the report of a patient who developed a *tuberculous meningitis* immediately after a chicken-pox infection.

**CHICKEN-POX AND HERPES ZOSTER.**—There have accumulated recently in the literature additional reports of patients with herpes zoster who, within a short time, developed varicella, and of persons who have been exposed to the former disease and contracted chicken-pox. B. Barling and J. Cahill (Brit M J 1 823 (May 3) 1930) observed 2 elderly patients who had a herpes ophthalmicus. One, aged 69 years, contracted chicken-pox 5 weeks later and the other, 80 years old, developed the disease 5 or 6 days after the onset of the herpes. There was no other known exposure and no history of previous drug treatment. A similar instance was

cited by R. R. McCormick (J A M A 96 766 (Mar 7) 1931). A patient 23 years old had a herpes zoster distributed over the skin area supplied by the lower thoracic nerves. Twelve days after the onset of this infection, a generalized vesicular eruption appeared which was diagnosed as chicken-pox. Within the following weeks, a generalized sepsis developed, with gangrene and hemorrhage in some of the lesions and the patient died. Necropsy revealed extensive hemorrhage and degeneration of the posterior nerve ganglia and the posterior horns of the spinal cord. The author had likewise observed 3 persons who developed herpes zoster following probable exposure to chicken-pox patients.

By means of complement fixation tests, A. Netter and A. Urbain (Ann de l'Inst Pasteur 46 17 (Jan) 1931) demonstrated a relationship between the 2 diseases. Using the blood serum of the patients, an antigen prepared from the fluid of chicken-pox lesions, or made from an emulsion of zoster crusts, these investigators observed a fixation of the complement. If vaccine lymph or an emulsion of impetigo crusts were used for an antigen, no fixation took place. In 100 patients with zoster, 93 per cent had specific antibodies in their blood serum. These antibodies are least in evidence at the onset of the eruption but reach the maximum quantity by about the end of the third week of the illness and are demonstrable for the succeeding 8 to 9 months.

**VARIOLA.** See SMALLPOX

**VULVOVAGINITIS, MONILIA.**—E. D. Plass, H. C. Hesseltine and I. H. Borts (Am J Obst and Gynec 21 320 (Mar) 1931) have found monilia frequently present in the

vaginal secretions of patients with vulvovaginitis, although normal women may harbor the fungi for long periods without showing vaginal irritation. Pregnancy and diabetes and probably menstruation are predisposing factors. Although children and virginal women may be affected, it will be found more frequently in parous women, although the mode of infection is unknown. High acidity of the vaginal secretion favors growth, but is not essential for its existence.

Itching and burning of the lower vagina and vulva, and painful coitus are the chief symptoms. A profuse

leukorrhea is rare. Occasionally the secretion is characteristic, containing small white flakes of thrush-like material. Monilia vaginitis tends to undergo spontaneous relief but occasionally becomes chronic.

Delivery usually brings complete relief in pregnant women, menstruation has the same effect in the nonpregnant. Alkaline douches and a 1 per cent aqueous solution of gentian violet applied locally afford the best treatment. Monilia vaginitis complicating the puerperium may be responsible for sporadic outbreaks of oral thrush in the newborn.

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## W

**WASSERMANN REACTION AND GYNECOLOGIC SURGERY.**—L. C. Scheffey (J. A. M. A 96 261 (Jan 24) 1931) reports that from 1923 to 1929 inclusive, there were 2622 admissions to the gynecologic service of Jefferson Medical College Hospital. Routine Wassermann tests were obtained in 2549 (97.2 per cent); 194 were positive, an incidence of 7.6 per cent.; 1064 cases were operative with a positive Wassermann reaction in 92 cases, an incidence of 8.6 per cent.

Preoperative complications, especially of the cardiovascular and nervous systems, are more likely to be present in patients exhibiting positive Wassermann reactions.

Patients with negative Wassermann reactions exhibited a higher degree of fertility. Abortions, premature labors and stillbirths (after the fourth month) were more pronounced in the positive Wassermann group. Systemic postoperative complications with recovery were of the same number and variety

in the 2 groups. The average number of postoperative hospital days showed practically no difference in the 2 groups or between the treated and untreated cases.

An investigation of the mortality rate in the positive Wassermann group showed it is similar to that of the entire series and of the negative cases as well (2.5 per cent).

Treatment prior to operation should not be indiscriminately advised or given as a matter of routine simply because the patient has a positive Wassermann reaction. Each case should be considered individually, the therapy employed being dependent on the amount of damage to the organism as a whole and not merely on the presence of syphilis. The author concludes that the patient with syphilis is not a greater risk simply because of the syphilitic infection. It is the amount of damage to the organism as a whole that is a vital factor concerned in evaluating the preoperative risk in such cases.



**WHOOPING-COUGH (PERTUSSIS).—DIAGNOSIS.**—

Although a leukocytosis and an increase in the percentage of lymphocytes is a very constant finding in patients with whooping-cough, it may not be present until the paroxysmal stage of the disease and is, therefore, of little value in early diagnosis. This point is stressed by L. W. Sauer and L. Hambrecht (*Am J Dis Child* 41 1327 (June) 1931). The average leukocyte counts of 70 patients demonstrated a leukopenia during the first week of the catarrhal stage, the number of white blood cells gradually rising during the second week, until it reached a peak at the end of the paroxysmal stage, usually about 6 weeks after the onset of symptoms. The number of cells declined to averages below normal during convalescence (eighth week of the disease). According to these statistics, most patients will have developed the typical paroxysms of the disease by the time the leukocytosis appears. Bearing in mind the fact that pertussis usually attacks infants or younger children who normally have rather high leukocyte counts with a preponderance of lymphocytes, the diagnostic value of leukocyte determinations in whooping-cough is even more doubtful. In a series of 25 children observed during their catarrhal stages, only 6 had true leukocytosis with a high lymphocytic ratio. The majority of a group of monkeys infected with pertussis bacilli had similar leukopenias at the onset and at the termination of the disease.

The same investigators (*J A M A* 95:263 (July 26) 1930) advocated another method for making an early and accurate diagnosis of pertussis. The procedure has been described previously by other workers. The patient coughs directly onto suitable culture media. A

petri dish is held 3 or 4 inches from the mouth of the patient and he is told to cough deeply in order to expel microorganisms from the larynx. In younger children the cough may be stimulated by touching the pharynx with a tongue blade or by giving them a drink of cold water or by exciting them in some manner. The plate is incubated and the colonies examined by the end of the second day. With this method, whooping-cough may be diagnosed before the lymphocytosis appears. Certain patients with the disease who never develop a typical whoop may be diagnosed also with this procedure. In a series of 200 patients, the plate method was positive in all but 53 during the catarrhal stage, in 65 per cent in the paroxysmal stage, and in none in the period of decline of symptoms.

Both the leukocyte counts and the petri dish methods were employed in making the diagnosis of pertussis by W. A. McGee (*J A M A* 97 922 (Sept 26) 1931), who reported that the total leukocyte and differential counts, together with the signs and symptoms, aided in the diagnosis in 78 instances in a group of 231 patients with whooping-cough. In 20 patients the diagnosis was aided by bacteriologic study. The latter method also helped to eliminate the diagnosis of the suspected disease in 32 instances.

In order to determine at once whether a person is suffering from whooping-cough, a typical paroxysm may be induced by spraying the pharynx with an irritating solution, according to K. Ochsenius (*München med. Wchnschr* 76 2167 (Dec 27) 1929). He employed a mixture of rectified oil of *turpentine* with 5 to 10 per cent of *eucalyptol*. This was sprayed into the throat with the result that portions of it were

inhaled by the child and frequently a typical paroxysm was produced in patients with whooping-cough

**COMPLICATIONS.**—In a series of experiments in which animals were given intravenous injections of endotoxin produced by *pertussis bacilli*, T Haya-kawa (Ztschr f Kinderh 47 532 (May) 1929) observed definite *lesions of the lungs*. These consisted chiefly of hyperemia of the interstitial tissue with a cellular reaction and edema. When large amounts of toxin were given, extravasated blood could occasionally be seen. The more acute disturbances in the vascular system found in the lungs of human patients with pertussis were thought to be due to the added acute congestion brought about by the paroxysms of coughing. The shadows observed in x-rays of lungs of pertussis patients might be explained by this interstitial reaction.

The typical shadows shown by x-rays of pertussis patients were described by O Gottche and G Eros (Monatschr f Kinderh 47 204, 1930). In 40 per cent of these patients they observed a 3-cornered shadow of the mediastinum which they thought represented enlarged *lymph glands* and the heart. There were thread-like shadows extending from the hilum to the diaphragm. In their opinion, the lymphatics which drain the peribronchial areas are especially involved in pertussis, and the hilar nodes, therefore, eventually bear the brunt of the burden of the infection. F Wildtgrube (Ztschr f Kinderh 50 152, 1930) discovered similar findings on the x-rays of pertussis patients, but not nearly so frequently. The radiating fine lines described by Gottche and Eros occurred in only 23 of a group of 107 patients, the triangular area in only 3 instances.

In a study of the pathologic changes in the *lungs* of 2 monkeys which had received injections of *pertussis bacilli* and had developed symptoms of the disease, and also of the lungs of a child who had died of pertussis at the age of 3 months, L W Sauer and L Hambrecht (Arch Path 8 944 (Dec) 1929) found most of the lesions in the smaller bronchi and bronchioles. Here were accumulations of debris consisting of epithelial cells, lymphocytes and polymorphonuclear leukocytes. Beneath the epithelium there was considerable lymphocytic infiltration. The *Bordet-Gengou bacillus* was found frequently in the bronchioles, in areas of beginning pneumonia.

**TREATMENT.**—Due to the absence of acceptable evidence as to the value of vaccines, either in preventing or curing patients with whooping-cough, the Council of the American Medical Association on Pharmacy and Chemistry decided to drop pertussis vaccines from the list of approved New and Nonofficial Remedies (J A M A 96 613 (Feb 21) 1931). However, clinical investigations with this material have continued and during the last few years, several favorable reports have appeared. The value of whooping-cough vaccine in the *prevention* of the disease was studied by R P Schowalter (Am J. Dis Child 39 544 (Mar) 1930). During the years 1921-26, institution children exposed to whooping-cough were given 1 c c (16 minims) of pertussis vaccine subcutaneously every second day for 4 doses. One c c (16 minims) of this vaccine contained 4,000,000 pertussis bacilli and 1,000,000,000 mixed microorganisms of other kinds. During 1927 and 1928 an ecto-antigen consisting of antigens of 3,000,000,000 bacteria was administered daily in 6 intramuscular doses varying from

0.5 c.c. (8 minims) at the beginning to 2 c.c. (32 minims) in succeeding injections. Comparing the statistics of the occurrence of whooping-cough in the institution during these 8 years of routine treatment with the 8 previous years when other prophylactic measures were used, the author concluded that the vaccine was of little value. The rate of incidence of pertussis was more than twice as great during the years vaccine was used as in the preceding period. The mortality rate, however, was about half as great in the years when treatment was used. The incidence of pertussis in the nearby city of Milwaukee was also greater during the last 8 years, as compared with the incidence in the preceding 8 years and the mortality from the disease was less in the later years.

Favorable reports of vaccine treatment of infants and children in the early stages of whooping-cough were made by W. Kaue (Med. Klin. 26:1740 (Nov. 21) 1930). He employed 4 intramuscular injections of vaccine at intervals of 3 or 4 days. The first vaccine injection contained 2,000,000,000 killed pertussis bacilli, the second 4,000,000,000, the third 6,000,000,000, and the fourth 8,000,000,000. In 8 children who contracted the disease the symptoms abated within 10 to 12 days after the treatment was started. In another group of 15 infants who were treated in the same manner, only 2 developed the disease and then only mild forms.

According to H. Pr  tet (Progr  s m  d. p. 193 (Jan. 31) 1931), a vaccine should agglutinate in serum of convalescent whooping-cough patients in dilutions of serum of 1:5000 to 1:10,000, the complement fixation reaction should be the same as that obtained with convalescent serum, and the vaccine should be given in a concentration of 750,000,-

000. In 48 pertussis patients treated with such a vaccine 34 were cured and 14 improved.

By growing strains of pertussis bacilli on a special medium, L. Mishulow, I. W. Mowry and E. B. Scott (J. Immunol. 19:227 (Aug.) 1930) produced a filtrate which was very toxic to rabbits. This could be used to immunize rabbits and their blood serum neutralized the toxin. When the toxin and the bacillus vaccine were given, rabbits produced agglutinins in their blood. Vaccines and toxins prepared by other methods with the ordinary media were not potent in producing these antibodies in rabbits.

Considerable optimism in regard to the **autogenous vaccine** treatment of pertussis was expressed by K. N. Kyriasid  s (Paris m  d. 2:473 (Nov. 30) 1929). He prepared the vaccine from the microorganisms found in nose and throat secretions of patients with the disease. Four or 5 days were required for the preparation and it was used in 33 patients during the first weeks of their illness. Favorable results were noted in regard to the alleviation of symptoms. Even when given in the second week of the disease to a group of children suffering from pulmonary complications, improvement in their condition was noted. Administration during the third week caused certain patients to cease having paroxysms but otherwise only about half of the group of 18 children were benefited by the vaccine. The **polyvalent vaccines** were thought to prevent or alleviate the complications in which the pertussis bacillus did not take part. In preparations of the autogenous vaccines, maximum temperatures of 131   F (55   C) were employed, so that the toxins of the microorganisms would not be totally destroyed, but were

preserved to exert their antigenic properties

N G Beliatzkaya and S I Kaplan-skaya (*Pediatriya* 13:370, 1929; *J. A. M. A.* 95 637 (Aug 23) 1930) combined a streptococcus vaccine with whooping-cough vaccine and concluded that, if given early, this treatment was very beneficial

Employing Besredka's method of inducing local tissue immunity to a disease, vaccine filtrates have been applied to pharyngeal mucous membranes by swabbing or by use of an atomizer S Kramezyk (*Monatschr. f. Kinderh.* 48 74, 1930) used filtrates of the pertussis bacillus and of other common microorganisms found in the pharynx The treatment was given daily for about a week and was very beneficial when started early in the course of the disease, sometimes entirely eliminating the paroxysmal stage

A few clinicians continue to observe beneficial results in the treatment of pertussis with the intramuscular injection of ether. J Levy and A S Finkelstein (*Arch. Pediat.* 46 762 (Dec) 1929) used 1 cc (16 minims) of ether with 1 cc (16 minims) of oil, giving 4 to 11 injections deep into the buttocks. Of a

group of 104 patients between the ages of 10 months and 2 years, 74 per cent were thought to be improved, 4 per cent slightly improved, and 22 per cent unimproved by the treatment In a few patients, double doses were given without harm, and it was believed that greater benefit followed

The comparative value of various methods of treatment of pertussis was observed in different groups of patients by W A McGee (*loc cit*), who concluded that rectal ether instillations produced the best results From the use of pertussis vaccines in 20 patients, ephedrine in 10 instances and cough sedatives in 14, he could arrive at no definite conclusions in regard to the distinctive value of any one of these drugs However, with rectal ether injections used exclusively in 121 patients and in combination with one of the above methods of treatment in 46 patients, improvement in symptoms was noted within 4 days' time as an average, as compared with 12 to 21 days with other methods The ether was mixed with equal parts of olive oil and given in doses of 4 cc (1 dram) for each year of age of the patient, twice daily, for 5 to 12 days.

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## X

### XANTHOMA, FAMILIAL.—

A review of the literature by U J. Wile and W. W Duemling (*Arch. Dermat. and Syph.* 21:642 (Apr.) 1930) reveals 14 instances of xanthomas involving members of the same family, the number comprising a total of 42 patients In 2 sisters affected, 1 showed mitral insufficiency which at postmortem proved to be due to xanthomas of the endocardium

Grenaud is cited as reporting in a review that the condition occurred about equally in both sexes. The age of patients on the appearance of lesions varied between birth and 40 years, with the greatest number beginning in patients between 3 and 6 years of age.

It has been shown that the lesions of xanthoma are not primarily due to a hypocholesteremia and that the high cholesterol content in the blood in the

lipemia of diabetes is merely an associated factor of the disordered fat metabolism. Unless the occurrence of the disease in members of the same family was merely accidental, it would have to be due primarily to a familial form of fat metabolism disorder.

The cases of 2 sisters reported herein tend, upon study, to conclusively show that the disease resulted from an apparent familial form of fat disorder due to potential diabetes. In both sisters a marked lipemia was found, circulating fat being present in the blood to the extent of 1383 and 1330 mg per 100 cc respectively. The cholesterol increase in the fat was much less than the increase in other fats. Dextrose tolerance in both showed a marked decrease below normal and prolonged studies established the fact that they apparently belonged in the group of potential diabetic patients.

A marked decrease in the number, consistency and size of the lesions could be achieved by a diet low in calories and was accompanied by a marked coincident decrease in the circulating lipemia. The lesions in these sisters occurred with a most extraordinarily symmetric distribution.

**X-RAY.—DIAGNOSIS.—In Gynecology.**—In discussing the use of pneumoperitoneum and lipiodol in pelvic diagnosis, I. F. Stein (Am J. Obst and Gynec 21: 671 (May) 1931) states that as proof of a successful Rubin test, the subdiaphragmatic meniscus may be demonstrated both fluoroscopically and roentgenographically. When iodized poppyseed oil or other radiopaque liquid is used, the Rubin test may be complemented or supplemented and the result recorded on an x-ray film. This is valuable in recording "spill" in cases

of tubal patency and in locating points of tubal obstruction, as well as indicating certain abnormalities of the uterine cavity.

Any intrauterine instillation is contraindicated in pregnancy because of the danger of abortion. With the employment of pneumoperitoneum and roentgenography, the female pelvic viscera may be clearly visualized so that any alterations of size or shape as well as tumors, adhesions and gestation may be recognized.

Stein advocates the use of both methods together, and claims that it is safe and simple. In his series of 530 cases of pneumoperitoneum and 200 cases in which iodized poppyseed oil and pneumoperitoneum were combined there were no accidents or complications.

**In Pelvic Disproportion.**—Herbert Thoms (Surg Gynec Obst 52: 963 (May) 1931) summarizes the methods used in the Yale University Clinic for determining disproportion between the fetus and the maternal pelvis. It is his opinion that to treat doubtful cases of disproportion without proper x-ray examination is as culpable as to treat fractures without the aid of the same diagnostic means.

By means of x-ray examination the obstetrician is able (1) to measure accurately both the anteroposterior and transverse diameters of the superior strait, and (2) by means of lateral pelvigrams, to outline the relationship of the promontory and anterior surface of the sacrum to the posterior surface of the symphysis pubis. This latter procedure is particularly useful in the patient in whom a rachitic pelvis is suspected. In patients at term it gives an excellent conception of the relationship of the presenting part to the pelvic brim.

He also emphasizes the importance of fetal cephalometry in considering the problem of disproportion. An intrauterine occipitofrontal diameter of 11.5 or over denotes a safely mature fetus. A diameter below 10.5 cm in length indicates that the fetus is premature.

X-ray mensuration of the pelvis should be carried out in all primiparous patients in whom disproportion is suspected.

***Of Intrauterine Death of Fetus.***

—On the basis of x-rays of fetuses that died before birth, E. Kehrer (Zentralbl. f. Gynak. 55:2530 (Aug. 22) 1931) concludes that there are certain signs from which death of the fetus may be suspected, and if several of them concur, they constitute conclusive evidence of intrauterine death. The most demonstrative signs of intrauterine death are the superposition of the flat cranial bones in the manner of roofing tile, the shriveling of the cranial contents, the occipital prolongation of the head in the shape of an isosceles triangle, and the sharp angular bending of the vertebral column in the form of kyphosis, lordosis or scoliosis. Especially demonstrative is a sort of givvous formation or a lordosis in the distal half, particularly in the sacral region of the vertebral column. All other x-ray signs that have been considered as indicative of intrauterine death of the fetus do not have absolute demonstrative value, since they may occur also in different conditions. These symptoms are asymmetry

of the cranium, flattening of the biparietal vault of the cranium, and the displacement of the face and the front of the fetus away from the center of the uterus and toward the wall of the uterus, with simultaneous deflection of the spinal column. The author considers the steep elevation of one arm behind the occiput, together with the lateral flexion and torsion of the cranium, as the earliest sign of intrauterine death, as a manifestation of the rigor mortis of the fetus, provided there are other signs that indicate death.

**THERAPEUTIC INDICATIONS.**—In reporting 380 cases of pelvic inflammatory disease treated by x-ray irradiation, L. Seitz (Strahlentherapie 37:595, 1930) states that in acute parametritis it aids absorption of the exudate or hastens abscess formation. Its chief indication is in the subacute and chronic cases of tubal inflammation or in parametritis.

About 75 per cent of the patients with gonorrhea respond favorably as indicated by a drop in the leukocyte count and a diminution of the erythrocyte sedimentation time.

The treatment is also effective in tubal disease of septic origin. Only 1 treatment is given, consisting of about 15 to 20 per cent of an erythema skin dose, so that the ovaries receive from  $\frac{1}{6}$  to  $\frac{1}{8}$  of a castration dose. In addition, conservative treatment in the form of hot douches is simultaneously employed.

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## Y

**YELLOW FEVER.—IMMUNITY DURATION.**—By experiments on rhesus monkeys, J. H. Bauer (Am. J. Trop. Med. 11:451 (Nov.) 1931)

determined that passive immunity to yellow fever by injection of immune serum lasts much longer if the immune serum is from an homologous species



than if it is derived from a foreign species

Human immune serum injected into the rhesus monkey gave passive immunity lasting less than 2 weeks, while rhesus monkey immune serum injected into the rhesus monkey produced a passive immunity which lasted usually over 4 weeks

It is assumed from the foregoing observations that man will receive a passive immunity to yellow fever which will be longer in duration if the immune serum is human in origin. This can not be proven experimentally in man, as the proof in the above experiments on monkeys required the death of many of the animals

Another advantage of homologous serum lies in the fact that repeated injections over varying periods of time do not cause anaphylaxis or serum sickness. Such repeated injections of immune serum are administered to laboratory workers who handle yellow fever virus

The amount of immune serum necessary to protect man from yellow fever infection is unknown, but 10 to 12 c c of convalescent serum is usually used prophylactically

Rhesus monkeys are not sufficiently uniform in their susceptibility to yellow fever to permit of their use for accurate titrations of the potency of immune serum on the basis of body weight

#### ACCIDENTAL INFECTION.—

It has been noted by G. P. Berry and S. I. Kitchen (*Ibid* 11:365 (Nov) 1931) that at least 32 accidental infections with yellow fever have occurred in laboratories in the past 4 years, and that only 4 laboratories of the 12 which are doing active research in yellow fever have escaped accidental infections. The infections have come

from contact with infectious monkey tissue and blood in the vast majority of cases. The bite of infective mosquitoes, contact with infected laboratory animals, and contact with infected mouse brain has accounted for most of the others. Five of the cases were fatal, many of the cases were mild

**CLINICAL FINDINGS.**—The cardinal signs of yellow fever, according to Berry and Kitchen (*Ibid*) are (1) paradoxical pulse—temperature relationship, (2) jaundice; (3) albuminuria, (4) black vomit. Of these symptoms, the increased temperature and decreased pulse rate (as slow as 50 per minute) were the only signs which were consistently present in all of 5 cases studied in the Hospital of the Rockefeller Institute for Medical Research in New York City. Therefore, the bradycardia was proven to occur independently of jaundice

Guanidine was increased in the blood of 1 mild case, indicating that there is extensive liver destruction in yellow fever in man, as has been demonstrated experimentally in monkeys

The leukocyte count falls progressively from the onset of the disease until the fifth day, when from 1500 to 2500 white cells are present per c m, with a relative increase of monocytes

It is important to note that convalescent human serum injected into laboratory workers at bimonthly intervals, in doses of 5 c c. will not prevent accidental infection

Virus exists in the blood in an unfixed state and such can be transferred to monkeys as late as the fifth day of the disease, neutralizing antibodies are present by the fourth day of the disease, as demonstrated by intraperitoneal inoculation in mice



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